STIC-ILL

10/006,401

From: Huynh, Phuong N.
Sent: Thursday, August 01, 2002 5:28 PM
To: STIC-ILL
Subject: RE: 10/006,401

4106539

Please deliver the following:

Clin Biochem Biol Res 321: 625-32; ~~1988~~ 1990 Progress Clin Biochem Biol Res 2326316

J Clin Invest 83(5): 1605-13; 1989

Pediatric research 20(9): 843-7; 1986

Proc Natl Acad Sci USA 83(17): 6543-7; 1986

J Biol Chem 269(6): 4401-08; 1994 7677780

Biochemical Medicine and metabolic Biology 46(3): 373-9; 1991

Clinica Chimica Acta 229(1-2): 99-106; 1994

Neurology 44(11): 2153-8; 1994

Thanks,
Neon
Art unit 1644
Mail 9E12
Tel 308-4844

Fatty Acid Oxidation: Clinical, Biochemical, and Molecular Aspects, pages 625–632

MOLECULAR CLONING AND NUCLEOTIDE SEQUENCE OF cDNAs ENCODING HUMAN SHORT CHAIN ACYL-CoA DEHYDROGENASE AND STUDY OF THE MOLECULAR BASIS OF HUMAN SHORT CHAIN ACYL-CoA DEHYDROGENASE DEFICIENCY

Etsuo Naito, Hisashi Ozasa, Yasuyuki Ikeda and Kay Tanaka
Yale University School of Medicine (E.N., K.T.), Department of Human Genetics, New Haven, CT 06510 USA; Tokyo Women's Medical College (H.O.), Tokyo, Japan and National Cardiovascular Center Research Institute (Y.I.), Osaka 565, Japan

INTRODUCTION

Short chain acyl-CoA dehydrogenase (SCAD) is a mitochondrial flavoprotein which catalyzes the first reaction in the ß-oxidation of short chain acyl-CoAs. It is one of the five acyl-CoA dehydrogenases that are currently known. Other enzymes in this group are medium chain acyl-CoA (MCAD), long chain acyl-CoA (LCAD), isovaleryl-CoA and 2-methyl-branched chain acyl-CoA dehydrogenases (1-3). Each of the acyl-CoA dehydrogenases is a homotetramer with a subunit molecular size of 40-45 kDa, containing 1 mol of FAD (1-3). All acyl-CoA dehydrogenases require electron transfer flavoprotein as an electron acceptor and share identical reaction mechanisms. However, they distinctly differ from each other in regard to the length and configuration of the hydrocarbon chain of the respective substrates. Their close functional and structural similarities suggest that the five acyl-CoA dehydrogenases may belong to a gene family (*acyl-CoA dehydrogenase family*), having evolved from a single ancestral gene (4).

Inherited SCAD deficiency has been recently reported in three infants by two groups of investigators (5-6). The main clinical features in two of them were metabolic acidosis and ethylmalonic aciduria. One of them died in the neonatal period with severe metabolic acidosis and hyperammonemia. The third patient had progressive skeletal muscle weakness, developmental delay, and muscle carnitine deficiency. Butyryl-CoA dehydrogenating activity in cultured fibroblasts from all three infants assayed in the presence of anti-MCAD antibody was less than 11% of the mean of controls.

As the first step in the study of the molecular basis of inherited SCAD deficiency and as a part of our study on the structure/function relationships and evolutionary aspects of the *acyl-CoA dehydrogenase family*, we cloned and sequenced cDNAs encoding the entire human precursor SCAD. In addition, we studied the protein and mRNA of the variant human SCAD and the restriction pattern of its gene in cultured skin fibroblasts from three patients with SCAD deficiency using a monospecific antibody and one of the isolated SCAD cDNA as probes. Details of this paper have been published elsewhere (7).

MATERIALS AND PROCEDURES

SCAD was previously purified to homogeneity from rat liver mitochondria (1) and postmortem human liver (8) in this laboratory. A polyclonal antiserum was raised in rabbit using the rat SCAD preparation as an antigen. The anti-SCAD antibody was monospecific, but recognized human SCAD. The sequences of the N-terminal region and 3 tryptic peptides of rat SCAD and the N-terminal sequence of human SCAD were determined by Dr. Ken Williams and Ms. Kathy Stone, Yale University School of Medicine and Dr. John Mole, University of Massachusetts Medical Center.

RESULTS

Molecular cloning of cDNA encoding human SCAD. Since the cross-reactivity of the anti-rat SCAD antibody to human SCAD was relatively weak, we first screened a rat liver cDNA library that was prepared in λgt11 expression vector using anti-rat SCAD antibody as a probe. After screening a half million plaques, five positive clones were isolated. One of them (RS-11) contained a 1041 bp insert. The predicted amino acid sequences in three portions of this insert perfectly matched the amino acid sequences of three tryptic peptides of rat SCAD (total: 57 amino acid residues), confirming that this clone encoded rat SCAD.

Using the RS-11 clone as a probe, we then screened approximately 250,000 recombinant phages from a human placental cDNA library prepared in λgt11 expression vector. After the secondary and tertiary screening, 13 putative human SCAD cDNA clones were isolated (7). A partial restriction map and sequence strategy of two of them (HS-1 and HS-12) are shown in Fig. 1. They were both approximately 1.8 kb in length. HS-1 was shifted 34 bases upstream, when compared to HS-12 (Fig. 1).

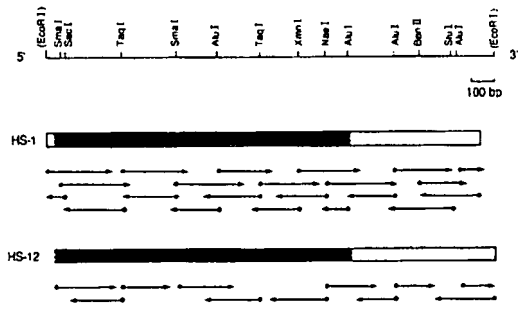

Fig. 1. Human short chain acyl-CoA dehydrogenase cDNA clones and sequencing strategy. Sections of the cDNA inserts that are shown with solid and open bars indicate the coding and non-coding regions, respectively. The cDNA inserts were digested with the indicted restriction enzymes. The fragments were subcloned into pGEM-blue and sequenced using T7 and SP6 promoter primers. The arrows indicate the direction and extent of DNA sequenced from each fragment. From Naito *et al* (7).

Nucleotide and amino acid sequences of human SCAD. Sequencing was done using HS-1 and HS-12. When combined, they covered nearly the entire length of human precursor SCAD (pSCAD) mRNA containing a 1,236 base pair coding region, which can be translated into a 412 amino acid protein, including a leader peptide (Fig. 2). With the exception of 3 discordant residues, the deduced amino acid sequence matched the amino terminal sequence and those of 3 tryptic peptides of the purified rat SCAD (total: 82 amino acid residues), confirming the identification of the cDNA as that of human SCAD. The 3 discordant amino acid residues are presumably due to species difference. In the N-terminal sequence analysis of human SCAD, the first residue could not be identified; presumably it was masked. The following 14 residues perfectly matched with the deduced sequence, except for Thr-37 which could not be unambiguously identified by peptide sequencing.

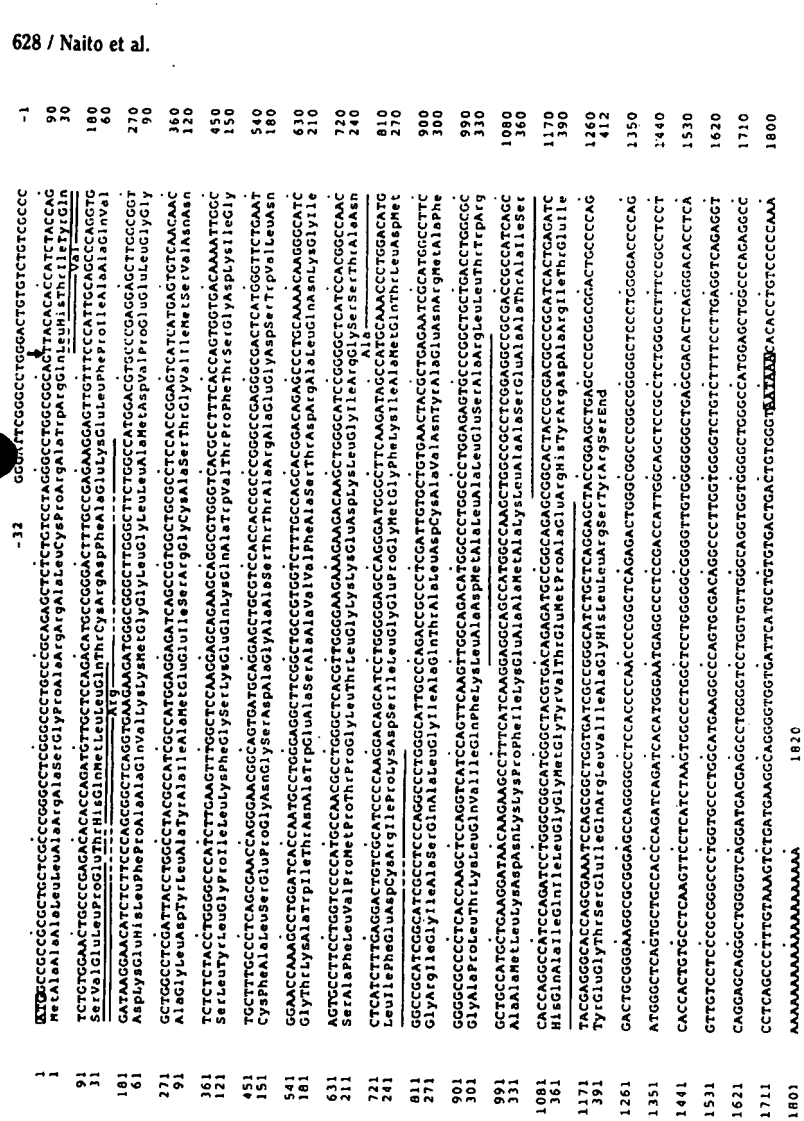

Fig. 2. Nucleotide and deduced amino acid sequences of the human short chain acyl-CoA dehydrogenase cDNAs. Regions underlined with light line matched the amino terminal (amino acid residues 25-51) and three internal tryptic peptide sequences derived from pure rat liver SCAD with the exception of 3 residues. The rat counterparts are shown under the discordant residues. The sequence underlined with a heavy line is that of purified human SCAD. Broken lines indicate equivocal amino acid assignments in peptide sequencing. The downward arrow between residues 24 and 25 indicates the cleavage site between the leader peptide and the mature protein. A possible polyadenylation signal in the 3'-untranslated region is boxed. From Naito *et al.* (7).

The calculated molecular size of human precursor pSCAD was 44,303. The cleavage site between the leader peptide and the mature protein was between residues 24 and 25 (Fig. 2). Thus, the sizes of the mature human SCAD and the leader peptide moiety were 41,727 (388 residues) and 2,576 (24 residues), respectively. The size of the purified human SCAD had been estimated to be 41 kDa by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) (1). The leader peptide contains five Arg residues and no acidic residues, rendering a positive charge, a characteristic feature commonly observed in the leader peptide of nuclear encoded mitochondrial enzymes (9).

Study of variant human SCAD. To characterize normal human SCAD in cultured skin fibroblasts, fibroblasts were labeled with [^{35}S]methionine, and cell lysates were analyzed by SDS-PAGE after immunoprecipitation using anti-rat SCAD antibody and Staphylococcus aureus cells (10). In normal cell lines, a major radioactive band with a molecular weight of 41 kDa was detected (Fig. 3, lane 1). This radioactive band was not detected when an excessive amount of pure rat SCAD was added prior to immunoprecipitation (competition experiment) (Fig. 3, lane 2), confirming that this band was indeed SCAD. In all three SCAD-deficient cell lines, a 41 kDa radioactive band identical in size to normal SCAD was detected. The intensities of the radioactive SCAD bands in the three SCAD-deficient cell lines were comparable to those of normal cell lines. These data suggest that the mutations in the three SCAD deficient patients are each a point mutation. More recently, we have obtained results which indicate that, in spite of the normal size of the variant SCAD in all three SCAD-deficient cell lines, their mutations are heterogeneous. When constitutive SCAD protein was analyzed by immunoblot analysis, cross-reactive material was negative in YH2065, while in the two other cell lines immunoreactive SCAD was detectable, indicating that the variant SCAD in YH2065 is extremely labile. The unstable nature of this variant SCAD was further confirmed by pulse-chase experiments (E. Naito and K. Tanaka, unpublished data).

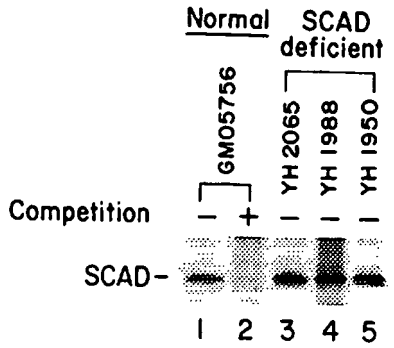

Fig. 3. Electrophoretic analysis of variant SCAD synthesized in three SCAD-deficient cells and controls. Lane 1: normal fibroblasts immunoprecipitated without the addition of pure rat SCAD; lane 2: normal fibroblasts immunoprecipitated after the addition of 7 μg of pure rat SCAD (competition experiment); lanes 3-5: three different SCAD-deficient cell lines. Cell line numbers are presented at the top of each lane. From Naito *et al.* (7).

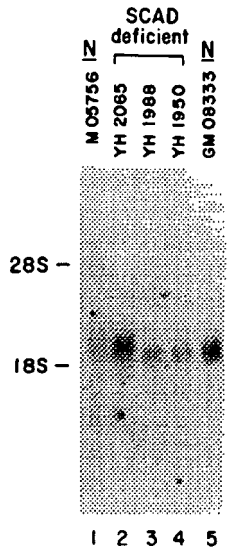

Fig. 4. Blot hybridization analysis of variant SCAD mRNA in three SCAD deficient cultured fibroblasts and two normal controls. Total RNA (20 μg) from each cell line was denatured by treatment with formamide and formaldehyde, and electrophoresed in a 1.0% agarose gel containing 2.2 M formaldehyde. The RNA was transferred to Hybond-N membrane and hybridized with the [^{32}P]labeled HS-1 probe. From Naito *et al.* (7).

Northern blot hybridization analysis of total RNAs isolated from two normal and three SCAD-deficient human fibroblasts was carried out using the HS-1 insert as a probe. A single 2.0 kb mRNA band kb of similar intensity was detected in all of them (Fig. 4). Genomic DNA from two normal and three SCAD-deficient fibroblast lines was digested with four restriction enzymes (*TaqI*, *BamHI*, *HincII* and *EcoRI*), and the fragments from each were subjected to blot hybridization analysis using radioactive HS-1 as a probe. In all the normal and SCAD-deficient cell lines, the lengths of the restriction fragments produced by these four enzymes were identical; digestion with *TaqI* or *BamHI* resulted in three bands each, whereas that with *HincII* produced two fragments. Two bands, 8.5 kb and 10.0 kb, were detected with *EcoRI* digestion (data not shown).

The observation, that there was no significant difference in the Northern or Southern blot analyses of control and SCAD-deficient fibroblasts, indicates that there were no gross deletions or rearrangements, and are consistent with the notion that the variants of SCAD in these cell lines are caused by a point mutation.

REFERENCES

1. Ikeda Y, Ikeda KO, Tanaka K (1985). Purification and characterization of short-chain, medium-chain, and long-chain acyl-CoA dehydrogenases from rat liver mitochondria. J Biol Chem 260:1311-1325.
2. Ikeda Y, Tanaka K (1983). Purification and characterization of isovaleryl coenzyme A dehydrogenase from rat liver mitochondria. J Biol Chem 258:1077-1085.
3. Ikeda Y, Tanaka K (1983). Purification and characterization of 2-methyl-branched chain acyl coenzyme A dehydrogenase, an enzyme involved in the isoleucine and valine metabolism, from rat liver mitochondria. J Biol Chem 258:9477-9487.
4. Tanaka K, Ikeda Y, Matsubara Y, Hyman DB (1987). Molecular basis of isovaleric acidemia and medium-chain acyl-CoA dehydrogenase deficiency. Enzyme 38:91-107.
5. Amendt BA, Green C, Sweetman L, Cloherty J, Shih V, Moon A, Teel L, Rhead WJ (1987). Short-chain acyl-coenzyme A dehydrogenase deficiency. Clinical and biochemical studies in two patients. J Clin Invest 79:1303-1309.
6. Coates PM, Hale DE, Finocchiaro G, Tanaka K, Winter SC (1988). Genetic deficiency of short-chain acyl-coenzyme A dehydrogenase in cultured fibroblasts from a patient with muscle carnitine deficiency and severe skeletal muscle weakness. J Clin Invest 81:171-175.

7. Naito E, Ozasa H, Ikeda Y, Tanaka K (1989). Molecular cloning and nucleotide sequence of complementary DNAs encoding human short chain acyl-coenzyme A dehydrogenase and the study of the molecular basis of human short chain acyl-coenzyme A dehydrogenase deficiency. J Clin Invest 83:1605-1613.
8. Finocchiaro G, Ito M, Tanaka K (1987). Purification and properties of short chain acyl-CoA, medium chain acyl-CoA, and isovaleryl-CoA dehydrogenases from human liver. J Biol Chem 262:7982-7989.
9. Hay R, Böhni P, Gasser S (1984). How mitochondria import proteins. Biochim Biophys Acta 779:65-87.
10. Ikeda Y, Keese SM, Fenton WA, Tanaka K (1985). Molecular heterogeneity of variant isovaleryl-CoA dehydrogenase from cultured isovaleric acidemia fibroblasts. Proc Natl Acad Sci USA 74:7081-7085.

Fatty Acid Oxidation: Clinical, Biochemical, and Molecular Aspects, pages 633–636

MOLECULAR CLONING AND NUCLEOTIDE SEQUENCE OF cDNA ENCODING THE RAT LONG CHAIN ACYL-CoA DEHYDROGENASE PRECURSOR

Yasuhiro Indo, Hisashi Ozasa, Yasuyuki Ikeda and Kay Tanaka

Yale University School of Medicine (Y.In., K.T.), Department of Human Genetics, New Haven, CT 06510 USA; Tokyo Women's Medical College (H.O.), Tokyo, Japan and National Cardiovascular Center Research Institute (Y.Ik.), Osaka 565, Japan

INTRODUCTION

Long chain acyl-CoA dehydrogenase (LCAD) is a mitochondrial flavoprotein that catalyzes the first reaction of the ß-oxidation mainly of fatty acids with 12 to 20 carbons (1,2). It is one of the five acyl-CoA dehydrogenases currently known (1, see the chapter on the purification of acyl-CoA dehydrogenases). The structural and functional similarities suggested that acyl-CoA dehydrogenases belong to a gene family (*the acyl-CoA dehydrogenase family*). Like other acyl-CoA dehydrogenases, LCAD is a homotetramer with a subunit size of 45 kDa (2). It is coded in the nucleus, synthesized in the cytosol as a precursor that is 3 kDa larger than the mature form, translocated into mitochondrial matrix and processed into the mature form (3).

Inherited LCAD deficiency in man was first identified in 1985. Its main clinical features are cardiorespiratory arrests during fasting, hepatomegaly, cardiomegaly and hypotonia, resulting in the death of patients in early infancy (4). As the first step in the investigation of the molecular basis of inherited LCAD deficiency and to provide data for the study of sequence homology among the enzymes in the *acyl-CoA dehydrogenase family*, we cloned and sequenced cDNAs encoding the LCAD precursor (pLCAD).

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1644PNH

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
NEWS 11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 12	Apr 08	"Ask CAS" for self-help around the clock
NEWS 13	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 14	Apr 09	ZDB will be removed from STN
NEWS 15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 19	Jun 03	New e-mail delivery for search results now available
NEWS 20	Jun 10	MEDLINE Reload
NEWS 21	Jun 10	PCTFULL has been reloaded
NEWS 22	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 23	Jul 19	NTIS to be reloaded July 28, 2002
NEWS 24	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 25	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 26	Jul 30	NETFIRST to be removed from STN

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:00:19 ON 01 AUG 2002

=> file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 12:00:30 ON 01 AUG 2002

FILE 'EMBASE' ENTERED AT 12:00:30 ON 01 AUG 2002

FILE 'BIOSIS' ENTERED AT 12:00:30 ON 01 AUG 2002

FILE 'SCISEARCH' ENTERED AT 12:00:30 ON 01 AUG 2002

FILE 'CAPLUS' ENTERED AT 12:00:30 ON 01 AUG 2002

=> s antibody
L1 2331124 ANTIBODY

=> s l1 and acyl coA dehydrogenase
L2 142 L1 AND ACYL COA DEHYDROGENASE

=> s l2 and human
L3 85 L2 AND HUMAN

=> dup remove l3
PROCESSING COMPLETED FOR L3
L4 34 DUP REMOVE L3 (51 DUPLICATES REMOVED)

=> d l4 1-34 cbib abs

L4 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2002 ACS
2002:315080 Document No. 136:336298 Sequences of a novel **human acyl-CoA dehydrogenase** sequence homolog and uses in diagnosis, therapy and drug screening. Xiao, Yonghong (Bayer Aktiengesellschaft, Germany). PCT Int. Appl. WO 2002033062 A1 20020425, 125 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-EP11872 20011015. PRIORITY: US 2000-PV240098 20001016; US 2000-PV258050 20001227.

AB The invention provides protein and cDNA sequences of a novel **human acyl-CoA dehydrogenase** sequence homolog. The invention also provides reagents and methods of regulating the expression or activities of the **human acyl-CoA dehydrogenase** sequence homolog. Reagents which regulate

human acyl-CoA dehydrogenase and reagents which bind to **human acyl-CoA dehydrogenase** gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, immune disorders, diabetes, obesity, and cancer.

L4 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2002 ACS

2002:315079 Document No. 136:336297 Protein and cDNA sequences of a novel **human acyl-CoA dehydrogenase** sequence homolog and diagnostic and therapeutic uses thereof. Kapeller-Libermann, Rosana; Hunter, John J.; Rudolph-Owen, Laura A. (Millennium Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2002033061 A2 20020425, 115 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US46720 20011022. PRIORITY: US 2000-PV242211 20001020.

AB The invention provides protein and cDNA sequences of a novel **human** protein, designated 32229, which has sequence homol. with **acyl-CoA dehydrogenase** members. The invention also provides antisense nucleic acid mols., recombinant expression vectors contg. 32229 nucleic acid mols., host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a 32229 gene has been introduced or disrupted. The invention still further provides isolated 32229 proteins, fusion proteins, antigenic peptides and anti-32229 **antibodies**. Diagnostic methods utilizing compns. of the invention are also provided.

L4 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2002 ACS

2002:256444 Document No. 136:275380 **Human** nucleic acids encoding oxidoreductases. Baughn, Mariah R.; Yue, Henry; Tribouley, Catherine M.; Lee, Ernestine A.; Hafalia, April J. A.; Sanjanwala, Madhu S.; Yao, Monique G.; Ding, Li; Elliott, Vicki S. (Incyte Genomics Inc., USA). PCT Int. Appl. WO 2002026951 A2 20020404, 117 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US30656 20010928. PRIORITY: US 2000-PV237101 20000929; US 2000-PV238482 20001006; US 2000-PV244024 20001027; US 2000-PV250805 20001201.

AB The invention provides eight **human** oxidoreductases (OXIRED) and polynucleotides which identify and encode OXIRED. The OXIRED proteins share sequence homol. with porcine 15-oxoprostaglandin 13-reductase, Deinococcus radiodurans **acyl-CoA dehydrogenase**, Salmonella typhimurium ribonucleoside diphosphate reductase, Lactococcus lactis 6-phosphogluconate dehydrogenase, bovine cytosolic dihydrodiol dehydrogenase, murine aldehyde dehydrogenase, **human** choline dehydrogenase, and a Caenorhabditis elegans phytoene desaturase homolog. The invention also provides expression vectors, host cells, **antibodies**, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders assocd. with aberrant expression of OXIRED, and in the assessment of the effect of exogenous compds. on the expression of nucleic acid and amino acid sequences of oxidoreductases.

L4 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2002 ACS
2002:285562 Document No. 137:61578 Expressed gene sets as markers for specific tumors. Ramaswamy, Sridhar; Golub, Todd B.; Tamayo, Pablo; Angelo, Michael (Whitehead Institute for Biomedical Research, USA; Danna-Farber Cancer Institute, Inc.). PCT Int. Appl. WO 2002024956 A2 20020328, 715 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-XB29287 20010919. PRIORITY: US 2000-PV233534 20000919; US 2001-PV278749 20010326; WO 2001-US29287 20010919.

AB Sets of genetic markers for specific tumor classes are described, as well as methods of identifying a biol. sample based on these markers. Total RNA was isolated from .apprx.300 **human** tumor and normal tissue specimens representing 30 individual classes of tumor or normal tissue, and cDNA produced using established mol. biol. protocols was hybridized to two high d. Affymetrix oligonucleotide microarrays (Hu6800FL and Hu35KsubA0). Raw expression data was combined into a master data set contg. the expression values for between 6800 and 16,000 genes expressed by each individual sample. A filter was applied to this data set which only allows those genes expressed at 3-fold above baseline and with an abs. difference in expression value of 100 to pass. By comparing the sets of genes which are expressed specifically in one class of tumor (e.g., pancreatic adenocarcinoma) vs. its accompanying normal tissue (e.g., normal pancreas), sets of genes were detd. which are specific to various tumors and their normal tissue counterparts. Also described are diagnostic, prognostic, and therapeutic screening uses for these markers, as well as oligonucleotide arrays comprising these markers. [This abstr. record is one of 4 records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L4 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2002 ACS
2002:51660 Document No. 136:98853 Proteins and nucleic acids associated with aging and their detection in identification of tissues undergoing senescence and of senescence modulators. Burmer, Glenna; Pritchard, David; Brown, Joseph P.; Demas, Vasiliki (Lifespan Biosciences, Inc., USA). PCT Int. Appl. WO 2002004662 A1 20020117, 70 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US21361 20010703. PRIORITY: US 2000-PV216470 20000706.

AB This invention relates to the discovery of nucleic acids and proteins assocd. with the aging processes, such as cell proliferation and senescence. The identification of these aging-assocd. nucleic acids and proteins have diagnostic uses in detecting the aging status of a cell population as well as applications for gene therapy and the delaying of the aging process.

L4 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2002 ACS
2001:763198 Document No. 135:328752 cDNA encoding **human** mutant medium chain **acyl-CoA dehydrogenase**, its

sequence, detection, modulation, biological and therapeutic uses. Black, Geooffrey D.; Wang, Yuee; Sun, Fei (Cellect Bio, Inc., USA). PCT Int. Appl. WO 2001077336 A2 20011018, 19 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US11685 20010410. PRIORITY: US 2000-PV195448 20000410.

AB The invention provides a cDNA mol. encoding a mutant **human** medium chain **acyl-CoA dehydrogenase** (mACADM), wherein compared to the wild-type cDNA, the mutant contains a 12-nucleotide insertion in the leader sequence, and a single nucleotide polymorphism (SNP) at position 1087. The invention also provides a host cell transformed with said **human** mACADM cDNA, and the use of said host cell in recombinant prodn. of **human** mACADM. The invention further provides methods for detecting, modulating and/or using the mACADM polypeptides and polynucleotides. Finally, the invention provides a method for: (1) diagnosing a disease or disorder assocd. with medium chain **acyl-CoA dehydrogenase** which involves using said mACADM polypeptides and polynucleotides, and (2) treating or preventing said disease using agents capable of interacting with mACADM polypeptides and polynucleotides. CDNA sequence (GenBank M16827 J05355) encoding the wild-type **human** ACADM was also provided in the invention.

L4 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2002 ACS

2001:416991 Document No. 135:29878 Protein and cDNA of a **human** ATP/GTP binding domain containing **acyl-CoA dehydrogenase** 11 and therapeutic use thereof. Mao, Yumin; Xie, Yi (Bioroad Gene Development Ltd. Shanghai, Peop. Rep. China). PCT Int. Appl. WO 2001040283 A1 20010607, 38 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Chinese). CODEN: PIXXD2. APPLICATION: WO 2000-CN495 20001127. PRIORITY: CN 1999-124150 19991129.

AB The invention provides cDNA sequences for a novel **human** ATP/GTP binding domain contg. **acyl-CoA dehydrogenase** 11 cloned from placenta brain, and its protein sequences. The invention also relates to constructing ATP/GTP binding domain contg. **acyl-CoA dehydrogenase** 11 gene expression vectors to prep. recombinant ATP/GTP binding domain contg. **acyl-CoA dehydrogenase** 11 protein using prokaryote or eukaryote cells. Methods of expressing and prepg. recombinant ATP/GTP binding domain contg. **acyl-CoA dehydrogenase** 11 protein and its **antibody** are described. Methods of using ATP/GTP binding domain contg. **acyl-CoA dehydrogenase** 11 gene or protein products for the treatment of various kinds of diseases, such as cancer, blood diseases, HIV infection, immune diseases and inflammation are also disclosed.

L4 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2002 ACS

2001:164276 Document No. 135:3762 Gene Cloning of Immunogenic Antigens Overexpressed in Pancreatic Cancer. Nakatsura, Tetsuya; Senju, Satoru; Yamada, Kazuhiro; Jotsuka, Toko; Ogawa, Michio; Nishimura, Yasuharu

(Division of Immunogenetics, Department of Neuroscience and Immunology, Kumamoto University Graduate School of Medical Sciences, Kumamoto, 860-0811, Japan). Biochemical and Biophysical Research Communications, 281(4), 936-944 (English) 2001. CODEN: BBRCA9. ISSN: 0006-291X. Publisher: Academic Press.

AB The serol. anal. of recombinant cDNA expression libraries (SEREX) by utilizing a library derived from a **human** pancreatic adenocarcinoma cell line and IgG **antibodies** from an allogeneic patient serum led to the identification of 18 genes: 13 of these were known genes, and 5 were unknown genes. In Northern and RT-PCR analyses, we found that the expression of mRNA of 14 genes was elevated in pancreatic cancer cell lines compared with the levels in normal pancreatic tissues. In addn., the expression of mRNA of hsp105 in colon cancer was greater than that in normal colon tissue. Immunohistochem. anal. using anti-hsp105 **antibody** revealed that an increased expression of hsp105 is a characteristic feature of pancreatic ductal and colon adenocarcinoma. Furthermore, hsp105 immunoreactivity in some cases of gastric, esophageal, and hepatocellular carcinoma was much stronger than that in normal corresponding tissues. These mols. identified may provide good diagnostic markers for cancer cells. (c) 2001 Academic Press.

L4 ANSWER 9 OF 34 MEDLINE DUPLICATE 1

2001038258 Document Number: 20517938. PubMed ID: 10913142. Cloning of a gene for an **acyl-CoA dehydrogenase** from Pisum sativum L. and purification and characterization of its product as an isovaleryl-CoA dehydrogenase. Reinard T; Janke V; Willard J; Buck F; Jacobsen H J; Vockley J. (LG Molekulargenetik, University of Hannover, Herrenhauser Strasse, D-30419 Hannover, Federal Republic of Germany.) JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Oct 27) 275 (43) 33738-43. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Isovaleryl-CoA dehydrogenase (IVD, EC) catalyzes the third step in the catabolism of leucine in mammals. Deficiency of this enzyme leads to the clinical disorder isovaleric acidemia. IVD has been purified and characterized from **human** and rat liver, and the x-ray crystallographic structure of purified recombinant **human** IVD has been reported. Nothing is known about IVD activity in plants, although cDNA clones from Arabidopsis thaliana and partial sequences from Gossypium hirsutum and Oryza sativa have been identified as putative IVDs based on sequence homology and immuno cross-reactivity. In this report we describe the identification and characterization of an IVD from pea, purification of the enzyme using a novel and rapid auxin affinity chromatography matrix, and cloning of the corresponding gene. At the amino acid level, pea IVD is 60% similar to **human** and rat IVD. The specific activity and abundance of plant IVD was found to be significantly lower than for its **human** counterpart and exhibits developmental regulation. Substrate specificity of the plant enzyme is similar to the **human** IVD, and it cross-reacts to anti-**human** IVD **antibodies**. Molecular modeling of the pea enzyme based on the structure of **human** IVD indicates a high degree of structural similarity among these enzymes. Glu-244, shown to function as the catalytic base in **human** IVD along with most of the amino acids that make up the acyl CoA binding pocket, is conserved in pea IVD. The genomic structure of the plant IVD gene consists of 13 exons and 12 introns, spanning approximately 4 kilobases, and the predicted RNA splicing sites exhibit the extended consensus sequence described for other plant genes.

L4 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2002 ACS

1999:468022 Document No. 131:99271 Cloning and cDNA sequence of **human** short-chain dehydrogenase. Lal, Preeti; Corley, Neil C. (Incyte Pharmaceuticals, Inc., USA). U.S. US 5928923 A 19990727, 27 pp. (English). CODEN: USXXAM. APPLICATION: US 1998-19216 19980205.

AB The invention provides a **human** short-chain dehydrogenase (HSCD) and polynucleotides which identify and encode HSCD. Nucleic acids encoding HSCD were first identified in Incyte clone 365351 from a prostate cDNA library using a computer search for amino acid sequence alignments; a consensus sequence was derived from overlapping and/or extended nucleic acid sequences. HSCD is 313 amino acids in length and has 4 potential casein kinase II phosphorylation sites, one potential glycosaminoglycan attachment site, one potential microbodies C-terminal targeting signal site, 4 potential N-myristoylation sites, and 5 potential protein kinase C phosphorylation sites, as well as chem. and structural homol. with short-chain **acyl-CoA dehydrogenase**.
Northern anal. shows the expression of this sequence in various libraries, at least 50% of which are immortalized or cancerous and .gtoreq.27% of which involve the immune response. The invention also provides expression vectors, host cells, **antibodies**, agonists, and antagonists. The invention also provides methods for treating or preventing disorders assocd. with expression of HSCD.

L4 ANSWER 11 OF 34 MEDLINE DUPLICATE 2
1998155203 Document Number: 98155203. PubMed ID: 9487154. **Human** long chain, very long chain and medium chain **acyl-CoA dehydrogenases** are specific for the S-enantiomer of 2-methylpentadecanoyl-CoA. Battaile K P; McBurney M; Van Veldhoven P P; Vockley J. (Mayo Clinic and Mayo Foundation, Department of Medical Genetics and Biochemistry/Molecular Biology, 200 First St, SW, Rochester, MN 55905, USA.) BIOCHIMICA ET BIOPHYSICA ACTA, (1998 Feb 23) 1390 (3) 333-8. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.
AB The **acyl-CoA dehydrogenases** are a family of mitochondrial flavoenzymes involved in fatty acid and branched chain amino-acid metabolism. Long chain **acyl-CoA dehydrogenase** (LCAD) and short/branched chain **acyl-CoA dehydrogenase** (SBCAD) have been shown to have activity towards 2-methyl branched chain acyl-CoA substrates of varying chain lengths. In **humans**, long chain 2-branched chain fatty acids such as pristanic acid are largely thought to be metabolized in peroxisomes through desaturation of their CoA esters by branched chain acyl-CoA oxidase, but LCAD is also capable of utilizing 2-methyldecanoyl- and 2-methylpalmitoyl-CoA as substrate [1]. Since the acyl-CoA oxidase reaction is specific for the S-enantiomer of the branched chain substrates, we investigated the stereo specificity of mitochondrial LCAD. Purified LCAD had a specific activity of 390 and 340 mU/mg of purified LCAD protein using palmitoyl-CoA and S-2-methylpentadecanoyl-CoA, respectively, as substrate. No activity was measurable with R-2-methylpentadecanoyl-CoA. Purified medium chain **acyl-CoA dehydrogenase** (MCAD) could also utilize S-2-methylpentadecanoyl-CoA as a substrate, but not R-2-methylpentadecanoyl-CoA. These results indicate that LCAD and MCAD are specific for the S-enantiomers of methylbranched chain substrates. Crude mitochondrial extracts showed no activity when dehydrogenating activity was measured with R/S-2-methylpalmitoyl-CoA or S-2-methylpentadecanoyl-CoA after inactivation of the extract with **antibodies** to very long chain **acyl-CoA dehydrogenase** and MCAD, suggesting that this substrate is not useful in identifyig clinical deficiencies of LCAD.

L4 ANSWER 12 OF 34 MEDLINE DUPLICATE 3
97322391 Document Number: 97322391. PubMed ID: 9177236. A role for Sp and nuclear receptor transcription factors in a cardiac hypertrophic growth program. Sack M N; Disch D L; Rockman H A; Kelly D P. (Department of Medicine, Washington University School of Medicine, St. Louis, MO 63110, USA.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED

STATES OF AMERICA, (1997 Jun 10) 94 (12) 6438-43. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB During cardiac hypertrophy, the chief myocardial energy source switches from fatty acid beta-oxidation (FAO) to glycolysis-a reversion to fetal metabolism. The expression of genes encoding myocardial FAO enzymes was delineated in a murine ventricular pressure overload preparation to characterize the molecular regulatory events involved in the alteration of energy substrate utilization during cardiac hypertrophy. Expression of genes involved in the thioesterification, mitochondrial import, and beta-oxidation of fatty acids was coordinately down-regulated after 7 days of right ventricular (RV) pressure overload. Results of RV pressure overload studies in mice transgenic for the promoter region of the gene encoding **human** medium-chain **acyl-CoA dehydrogenase** (MCAD, which catalyzes a rate-limiting step in the FAO cycle) fused to a chloramphenicol acetyltransferase reporter confirmed that repression of MCAD gene expression in the hypertrophied ventricle occurred at the transcriptional level. Electrophoretic mobility-shift assays performed with MCAD promoter fragments and nuclear protein extracts prepared from hypertrophied and control RV identified pressure overload-induced protein/DNA interactions at a regulatory unit shown previously to confer control of MCAD gene transcription during cardiac development. **Antibody** "supershift" studies demonstrated that members of the Sp (Sp1, Sp3) and nuclear hormone receptor [chicken ovalbumin upstream promoter transcription factor (COUP-TF)/erbA-related protein 3] families interact with the pressure overload-responsive unit. Cardiomyocyte transfection studies confirmed that COUP-TF repressed the transcriptional activity of the MCAD promoter. The DNA binding activities and nuclear expression of Sp1/3 and COUP-TF in normal fetal mouse heart were similar to those in the hypertrophied adult heart. These results identify a transcriptional regulatory mechanism involved in the reinduction of a fetal metabolic program during pressure overload-induced cardiac hypertrophy.

L4 ANSWER 13 OF 34 MEDLINE

1998008000 Document Number: 98008000. PubMed ID: 9345094.

D-3-hydroxyacyl-CoA dehydratase/D-3-hydroxyacyl-CoA dehydrogenase bifunctional protein deficiency: a newly identified peroxisomal disorder. Suzuki Y; Jiang L L; Souri M; Miyazawa S; Fukuda S; Zhang Z; Une M; Shimozawa N; Kondo N; Orii T; Hashimoto T. (Department of Pediatrics, Gifu University School of Medicine, Gifu, Japan.. ysuz@cc.gifu-u.ac.jp) . AMERICAN JOURNAL OF HUMAN GENETICS, (1997 Nov) 61 (5) 1153-62. Journal code: 0370475. ISSN: 0002-9297. Pub. country: United States. Language: English.

AB Peroxisomal beta-oxidation proceeds from enoyl-CoA through D-3-hydroxyacyl-CoA to 3-ketoacyl-CoA by the D-3-hydroxyacyl-CoA dehydratase/D-3-hydroxy-**acyl-CoA dehydrogenase** bifunctional protein (d-bifunctional protein), and the oxidation of bile-acid precursors also has been suggested as being catalyzed by the d-bifunctional protein. Because of the important roles of this protein, we reinvestigated two Japanese patients previously diagnosed as having enoyl-CoA hydratase/L-3-hydroxyacyl-CoA dehydrogenase bifunctional protein (L-bifunctional protein) deficiency, in complementation studies. We found that both the protein and the enzyme activity of the d-bifunctional protein were hardly detectable in these patients but that the active L-bifunctional protein was present. The mRNA level in patient 1 was very low, and, for patient 2, mRNA was of a smaller size. Sequencing analysis of the cDNA revealed a 52-bp deletion in patient 1 and a 237-bp deletion in patient 2. This seems to be the first report of D-bifunctional protein deficiency. Patients previously diagnosed as cases of L-bifunctional protein deficiency probably should be reexamined for a possible d-bifunctional protein deficiency.

L4 ANSWER 14 OF 34 MEDLINE DUPLICATE 4

96315628 Document Number: 96315628. PubMed ID: 8754802. Transcriptional control of a nuclear gene encoding a mitochondrial fatty acid oxidation enzyme in transgenic mice: role for nuclear receptors in cardiac and brown adipose expression. Disch D L; Rader T A; Cresci S; Leone T C; Barger P M; Vega R; Wood P A; Kelly D P. (Department of Medicine, Washington University School of Medicine, St. Louis, Missouri, USA.) MOLECULAR AND CELLULAR BIOLOGY, (1996 Aug) 16 (8) 4043-51. Journal code: 8109087. ISSN: 0270-7306. Pub. country: United States. Language: English.

AB Expression of the gene encoding medium-chain acyl coenzyme A dehydrogenase (MCAD), a nuclearly encoded mitochondrial fatty acid beta-oxidation enzyme, is regulated in parallel with fatty acid oxidation rates among tissues and during development. We have shown previously that the **human** MCAD gene promoter contains a pleiotropic element (nuclear receptor response element [NRRE-1]) that confers transcriptional activation or repression by members of the nuclear receptor superfamily. Mice transgenic for **human** MCAD gene promoter fragments fused to a chloramphenicol acetyltransferase gene reporter were produced and characterized to evaluate the role of NRRE-1 and other promoter elements in the transcriptional control of the MCAD gene in vivo. Expression of the full-length MCAD promoter-chloramphenicol acetyltransferase transgene (MCADCAT.371) paralleled the known tissue-specific differences in mitochondrial beta-oxidation rates and MCAD expression. MCADCAT.371 transcripts were abundant in heart tissue and brown adipose tissue, tissues with high-level MCAD expression. During perinatal cardiac developmental stages, expression of the MCADCAT.371 transgene paralleled mouse MCAD mRNA levels. In contrast, expression of a mutant MCADCAT transgene, which lacked NRRE-1 (MCADCATdeltaNRRE-1), was not enriched in heart or brown adipose tissue and did not exhibit appropriate postnatal induction in the developing heart. Transient-transfection studies with MCAD promoter-luciferase constructs containing normal or mutant NRRE-1 sequences demonstrated that the nuclear receptor binding sequences within NRRE-1 are necessary for high-level transcriptional activity in primary rat cardiocytes. Electrophoretic mobility shift assays demonstrated that NRRE-1 was bound by several cardiac and brown adipose nuclear proteins and that these interactions required the NRRE-1 receptor binding hexamer sequences. **Antibody** supershift studies identified the orphan nuclear receptor COUP-TF as one of the endogenous cardiac proteins which bound NRRE-1. These results dictate an important role for nuclear receptors in the transcriptional control of a nuclear gene encoding a mitochondrial fatty acid oxidation enzyme and identify a gene regulatory pathway involved in cardiac energy metabolism.

L4 ANSWER 15 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

1995:123570 Document No.: PREV199598137870. Isoalloxazine Ring of FAD Is Required for the Formation of the Core in the Hsp60-assisted Folding of Medium Chain **Acyl-CoA Dehydrogenase** Subunit into the Assembly Competent Conformation in Mitochondria. Saijo, Takahiko; Tanaka, Kay (1). (1) Dep. Genetics, Yale Univ. Sch. Med., 333 Cedar St., P.O. Box 3333, New Haven, CT 06510 USA. Journal of Biological Chemistry, (1995) Vol. 270, No. 4, pp. 1899-1907. ISSN: 0021-9258. Language: English.

AB We studied the role of FAD in the intramitochondrial folding and assembly of medium-chain **acyl-CoA dehydrogenase** (MCAD), a homotetrameric mitochondrial enzyme containing a molecule of non-covalently bound FAD/monomer. In the MCAD molecule, FAD is buried in a crevice containing the active center. We have previously shown that upon import into mitochondria, newly processed MCAD is first incorporated into a high molecular weight (hMr) complex and that the hMr complex mainly consisted of MCAD-heat-shock protein 60 (hsp60) complex (Saijo, T., Welch, W. J., and Tanaka, K (1994) J. Biol. Chem. 269, 4401-4408). In the present study, we incubated in vitro synthesized precursor MCAD with mitochondria isolated from normal and riboflavin-deficient rat liver for 10-60 min and fractionated the solubilized mitochondria using gel filtration. The amount of MCAD in the hMr complex was larger and that of tetramer was smaller in

riboRavin-deficient mitochondria than in control at any time point. In addition, riboflavin-deficient mitochondria were solubilized after 10-min import in a buffer containing ATP and were chased in the presence of FAD, FMN, or NAD+ or without any addition. The mitochondrial proteins were analyzed using gel filtration or immunoprecipitated with anti-hsp60 **antibody**. After 60-min chase in the presence of FAD, the majority of MCAD in the complex with hsp60 was transferred to tetramer, whereas no such transfer occurred after the chase in the absence of FAD. When chase was done in the presence of FMN, a significant amount of MCAD was transferred from the complex with hsp60 to tetramer, but the transfer was not as efficient as in the presence of FAD. The chase in the presence of NAD+ resulted in no transfer. These data suggest that isoalloxazine ring of FAD plays a critical role, exerting nucleating effect, in the hsp60-assisted folding of MCAD subunit into an assembly competent conformation, probably assisting the formation of the core.

L4 ANSWER 16 OF 34 MEDLINE DUPLICATE 5

95294701 Document Number: 95294701. PubMed ID: 7776094. Clinical and biochemical characterization of short-chain acyl-coenzyme A dehydrogenase deficiency. Bhala A; Willi S M; Rinaldo P; Bennett M J; Schmidt-Sommerfeld E; Hale D E. (Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, USA.) JOURNAL OF PEDIATRICS, (1995 Jun) 126 (6) 910-5. Journal code: 0375410. ISSN: 0022-3476. Pub. country: United States. Language: English.

AB OBJECTIVE: We identified two additional patients with short-chain acyl-coenzyme A (CoA), further characterized the clinical and biochemical features of this defect, and compared it with other fatty acid oxidation defects. DESIGN: We have measured the in vitro short-chain acyl-coenzyme A dehydrogenase (SCAD) activity in six affected persons with the electron-transfer flavoprotein-linked assay in the presence and absence of anti-medium-chain **acyl-CoA dehydrogenase antibody**. Urine organic acids, acylglycines, acylcarnitines, and radiolabeled substrate catabolism by skin fibroblasts were also examined. RESULTS: All patients had some neurologic abnormalities, including hypotonia, hypertonia, or seizures. None of the patients had episodes of hypoglycemia; in the only patient tested, fasting ketogenesis was not impaired. Four patients were initially seen in the neonatal period, two with profound metabolic acidosis and two with mild acidemia; the other two cases were recognized in infancy. Enzymatic analysis of cultured skin fibroblasts demonstrated approximately 10% activity of SCAD when compared with control fibroblasts. Gas chromatography and mass spectrometry of urine revealed that ethylmalonic acid was present in all samples but not always at elevated concentrations; methylsuccinic acid and butyrylglycine were sporadically elevated. n-Butyrylcarnitine was often found in urine and plasma. Radiolabeled substrate metabolism was reduced to 40% to 60% of control values. CONCLUSIONS: Because affected persons do not consistently excrete characteristic metabolites, the diagnosis of this enzymatic deficiency is difficult. It is necessary to collect and analyze several urine and plasma specimens when the diagnosis is being considered in patients with neurologic abnormalities suggestive of this disorder.

L4 ANSWER 17 OF 34 MEDLINE

94140872 Document Number: 94140872. PubMed ID: 7905878. Intramitochondrial folding and assembly of medium-chain **acyl-CoA dehydrogenase** (MCAD). Demonstration of impaired transfer of K304E-variant MCAD from its complex with hsp60 to the native tetramer. Saijo T; Welch W J; Tanaka K. (Department of Genetics, Yale University School of Medicine, New Haven, Connecticut 06510.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Feb 11) 269 (6) 4401-8. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB We incubated in vitro translated precursor of medium-chain **acyl-CoA dehydrogenase** (MCAD) with isolated rat liver mitochondria and fractionated the solubilized mitochondria on gel

filtration. After a 5-min import into mitochondria, MCAD was recovered exclusively as a high molecular weight (hMr) complex (700,000), while after a 10-min import, it was recovered mainly in the hMr complex and mature tetramer, with a small amount in monomer. Either a further 15-min chase or exposure to ATP caused a marked decrease of MCAD in the hMr complex and an increase in the mature tetramer in comparable amounts, suggesting that the hMr complex was the precursor of tetramer. No monomer was detected in either case. Using specific **antibodies**, we have shown that the hMr complex represented a complex of MCAD and heat-shock protein 60 (hsp60), and, that upon import into mitochondria, unfolded MCAD first formed a transient complex with mitochondrial heat-shock protein 70 (hsp70mit) and then transferred to hsp60 to complete its folding into an assembly-competent conformation. We also examined the assembly of K304E MCAD, which is a prevalent variant enzyme among patients with MCAD deficiency. The assembly of the K304E into its tetrameric form was severely impaired. The binding of K304E with hsp70mit and its transfer from hsp70mit to hsp60 were normal. However, the hsp60 complex of K304E was much more stable than the wild-type counterpart upon a 15-min chase or exposure to ATP, suggesting that the folding in, or the transfer of K304E subunit to tetramer from, the complex with hsp60 was impaired.

L4 ANSWER 18 OF 34 MEDLINE DUPLICATE 6

95060008 Document Number: 95060008. PubMed ID: 7969976. Late-onset riboflavin-responsive myopathy with combined multiple acyl coenzyme A dehydrogenase and respiratory chain deficiency. Antozzi C; Garavaglia B; Mora M; Rimoldi M; Morandi L; Ursino E; DiDonato S. (Neuromuscular Research Center, Istituto Nazionale Neurologico C. Besta, Milan, Italy.) NEUROLOGY, (1994 Nov) 44 (11) 2153-8. Journal code: 0401060. ISSN: 0028-3878. Pub. country: United States. Language: English.

AB We studied the effect of riboflavin treatment on the clinical status and on the activities of beta-oxidation and respiratory chain enzymes in a 69-year-old patient with late-onset myopathy. Before treatment, she was very weak and wasted in the limbs and trunk muscles; also, she could not walk or attend to daily activities. Marked lipid storage was present in the muscle biopsy. The activities of short-chain acyl coenzyme A (**acyl-CoA**) **dehydrogenase** (SCAD), medium-chain **acyl-CoA dehydrogenase** (MCAD), and long-chain **acyl-CoA dehydrogenase** (LCAD) in isolated muscle mitochondria were reduced to less than 10% of control values. This defect in fatty acid oxidation was associated with a marked deficiency of two flavin-dependent respiratory chain complexes: complex I activity was 20% and complex II activity was 25% of control values. By contrast, the activities of the nonflavin-dependent complex III and complex IV were normal. Western blot analysis of the patient's muscle mitochondrial extracts with **antibodies** raised against purified SCAD, MCAD, and the alpha- and beta-subunits of the electron transfer flavoprotein (ETF) showed absence of SCAD cross-reacting material (CRM), markedly decreased MCAD-CRM, and normal amounts of both alpha- and beta-ETF-CRM. After riboflavin treatment, the patient's clinical status dramatically improved and morphologic changes in muscle disappeared. SCAD activity increased to 55% of control values, whereas MCAD, LCAD, and complex I and complex II activities normalized. SCAD and MCAD immunoreactivity was restored to normal. On the basis of our experience and the data in the literature, we concluded that some lipid storage myopathies can show dramatic response to riboflavin.

L4 ANSWER 19 OF 34 MEDLINE DUPLICATE 7

95079671 Document Number: 95079671. PubMed ID: 7988059. Measurement of short-chain **acyl-CoA dehydrogenase** (SCAD) in cultured skin fibroblasts with hexanoyl-CoA as a competitive inhibitor to eliminate the contribution of medium-chain **acyl-CoA dehydrogenase**. Niezen-Koning K E; Wanders R J; Nagel G T; Sewell A C; Heymans H S. (Department of Pediatrics, University Hospital Groningen,

The Netherlands.) CLINICA CHIMICA ACTA, (1994 Sep) 229 (1-2) 99-106. Journal code: 1302422. ISSN: 0009-8981. Pub. country: Netherlands. Language: English.

AB Short-chain **acyl-CoA dehydrogenase** (SCAD) deficiency has so far been reported in only very few patients. This is due, in part, to the problems involved in measuring the activity of SCAD unequivocally. The main reason for this difficulty is that butyryl-CoA, the substrate preferably used for SCAD activity measurements, is also dehydrogenated by medium-chain **acyl-CoA dehydrogenase** (MCAD). Elimination of this contribution can be achieved by means of immune precipitation with a specific MCAD **antibody**. We now describe a relatively straightforward assay based on the use of gas chromatography/mass spectrometry for detection. The contribution of MCAD to overall butyryl-CoA dehydrogenation was eliminated by adding excess hexanoyl-CoA to the assay medium. The validity of the method developed was checked by SCAD-activity measurements in fibroblasts from an established SCAD-deficient patient.

L4 ANSWER 20 OF 34 MEDLINE DUPLICATE 8

93221511 Document Number: 93221511. PubMed ID: 8466512. A novel disease with deficiency of mitochondrial very-long-chain **acyl-CoA dehydrogenase**. Aoyama T; Uchida Y; Kelley R I; Marble M; Hofman K; Tonsgard J H; Rhead W J; Hashimoto T. (Department of Biochemistry, Shinshu University School of Medicine, Nagano, Japan.) BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1993 Mar 31) 191 (3) 1369-72. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Palmitoyl-CoA dehydrogenase activity in skin fibroblasts from seven patients with unidentified defects of fatty acid oxidation was measured in the presence and absence of **antibodies** against medium-chain, long-chain, and very-long-chain **acyl-CoA dehydrogenases** (VLCAD). Two of the patients, 4-5 month old boys, were found to have a novel disease, VLCAD deficiency, as judged from the results of very low palmitoyl-CoA dehydrogenase activity and the lack of immunoreactivity toward **antibody** raised to purified VLCAD.

L4 ANSWER 21 OF 34 SCISEARCH COPYRIGHT 2002 ISI (R)

92:301429 The Genuine Article (R) Number: HT004. STRUCTURAL AND REDOX RELATIONSHIPS BETWEEN PARACOCCUS-DENITRIFICANS, PORCINE AND **HUMAN** ELECTRON-TRANSFERRING FLAVOPROTEINS. WATMOUGH N J; KISS J; FRERMAN F E (Reprint). UNIV COLORADO, SCH MED, DEPT PEDIAT, BF STOLINSKY LABS, BOX C233, 4200 E 9TH AVE, DENVER, CO, 80262. EUROPEAN JOURNAL OF BIOCHEMISTRY (01 MAY 1992) Vol. 205, No. 3, pp. 1089-1097. ISSN: 0014-2956. Pub. country: USA. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Electron-transferring flavoprotein (ETF) was purified from the bacterium Paracoccus denitrificans and the structural and redox relationships to the porcine and **human** ETFs were investigated. The three proteins have essentially identical subunit masses and the alpha-helix content of the bacterial and porcine ETFs are very similar, indicating global structural similarity. An anti-(porcine ETF) polyclonal **antibody** that crossreacts with the **human** large and small subunits also crossreacts strongly with the large subunit of Paracoccus ETF. However, crossreactivity with the small subunit is very weak. Nonetheless, an amino-terminal peptide and four internal peptides of the small bacterial subunit show extensive sequence identity with the **human** small subunit. Local similarities in environment are also indicated by the intrinsic tryptophan fluorescence emission spectra of porcine and Paracoccus ETFs.

Although the visible spectra of porcine and Paracoccus ETFs are virtually identical, flavin fluorescence in the bacterial protein is only 15% that of the mammalian protein. Further, the circular dichroic spectrum of the flavin in the bacterial protein is significantly more intense,

suggesting that the microenvironment of the isoalloxazine ring is different in the two proteins.

Enzymatic or photochemical reduction of Paracoccus ETF rapidly yields an anionic semiquinone; formation of the fully reduced flavin in the bacterial ETF is very slow. The spacing of the oxidation-reduction potentials of the flavin couples in the bacterial ETF is essentially identical to that in porcine ETF as judged from the disproportionation equilibrium of the bacterial ETF flavin semiquinone. Together, the enzymatic reduction and disproportionation equilibria suggest that the flavin potentials of the two ETFs must be very close.

The data indicate that the structural properties of the bacterial and mammalian proteins and the thermodynamic properties of the flavin prosthetic group of the proteins are very similar.

L4 ANSWER 22 OF 34 MEDLINE DUPLICATE 9

92278874 Document Number: 92278874. PubMed ID: 1594327. Immunochemical characterization of variant medium-chain **acyl-CoA dehydrogenase** in fibroblasts from patients with medium-chain **acyl-CoA dehydrogenase** deficiency. Coates P M; Indo Y; Young D; Hale D E; Tanaka K. (Division of Gastroenterology/Nutrition, Children's Hospital of Philadelphia, PA 19104.) PEDIATRIC RESEARCH, (1992 Jan) 31 (1) 34-8. Journal code: 0100714. ISSN: 0031-3998. Pub. country: United States. Language: English.

AB Medium-chain **acyl-CoA dehydrogenase** (MCAD) deficiency is a common autosomal recessive disorder of mitochondrial fatty acid oxidation characterized by episodes of hypoketotic hypoglycemia usually beginning in the first 2 y of life. We previously showed, in pulse labeling experiments, that the biosynthesis and immediate posttranslational processing of MCAD are normal in fibroblasts from patients with MCAD deficiency. Most patients studied to date are homozygous for a point mutation (A985-G) that results in the substitution of glutamate for lysine ar residue 304 of the mature MCAD subunit. We performed immunoblot analysis of fibroblast MCAD from a total of 34 patients with MCAD deficiency, including 31 homozygous for the A985-G mutation, using a rabbit anti-rat MCAD **antibody** that cross-reacted specifically with **human** MCAD, but not with the related enzymes, short-chain and long-chain **acyl-CoA dehydrogenases**. All patients with the A985-G mutation lacked detectable MCAD. Pulse-chase labeling of MCAD-deficient fibroblasts with 35S-methionine demonstrated that this variant MCAD was unstable compared to controls. Taken together, these data suggest that this mutation affects the stability of MCAD protein within the mitochondrial matrix.

L4 ANSWER 23 OF 34 MEDLINE

91302334 Document Number: 91302334. PubMed ID: 1830048. The beta-oxidation system in catalase-free microbodies of the filamentous fungus Neurospora crassa. Purification of a multifunctional protein possessing 2-enoyl-CoA hydratase, L-3-hydroxyacyl-CoA dehydrogenase, and 3-hydroxyacyl-CoA epimerase activities. Thieringer R; Kunau W H. (Institut fur Physiologische Chemie, Abteilung fur Zellbiochemie, Ruhr-Universitat Bochum, Federal Republic of Germany.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Jul 15) 266 (20) 13110-7. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB A trifunctional beta-oxidation protein, designated TFP, was purified to apparent homogeneity from oleate-induced mycelia of Neurospora crassa. 2-Enoyl-CoA hydratase, L-3-hydroxyacyl-CoA dehydrogenase, and 3-hydroxyacyl-CoA epimerase activities copurified in constant ratios with this protein when crude extracts were subjected to cation-exchange, dye-ligand, and adsorption chromatography. Trifunctionality was substantiated by coinciding enzyme activity ratios during the last two purification steps and additional chromatographic steps. The enzyme was shown to be a 365-kDa tetramer of subunits with a molecular mass of 93 kDa. Several lines of evidence suggest that these subunits are identical.

Monospecific **antibodies** raised against the homogenous protein specifically precipitated the three enzymatic activities of TFP. Immunoblotting of fractions obtained after sucrose density gradient centrifugation of a crude extract indicated that TFP was exclusively localized in glyoxysome-like microbodies. The beta-oxidation system of N. crassa is structurally related to those of peroxisomes despite the presence of an **acyl-CoA dehydrogenase** rather than an acyl-CoA oxidase. A mitochondrial 2-enoyl-CoA hydratase activity was separated from TFP and purified to apparent homogeneity. The absence of all other beta-oxidation activities from mitochondria suggests that this organelle and its 2-enoyl-CoA hydratase are not involved in fatty acid degradation in N. crassa.

L4 ANSWER 24 OF 34 MEDLINE DUPLICATE 10

92172480 Document Number: 92172480. PubMed ID: 1793614. Immunoreactive enzyme protein in medium-chain **acyl-CoA dehydrogenase** deficiency. Ogilvie I; Jackson S; Bartlett K; Turnbull D M. (Division of Clinical Neuroscience, Medical School, University of Newcastle upon Tyne, United Kingdom.) BIOCHEMICAL MEDICINE AND METABOLIC BIOLOGY, (1991 Dec) 46 (3) 373-9. Journal code: 8605718. ISSN: 0885-4505. Pub. country: United States. Language: English.

AB Medium-chain **acyl-CoA dehydrogenase** (MCAD) deficiency is a common inborn error of mitochondrial fatty acid oxidation. To determine if immunoreactive enzyme protein is present in patients with MCAD deficiency, we studied cultured skin fibroblasts from patients with the 985 point mutation, present in about 85% of cases, and cell lines from patients in which the point mutation is not present or only involves one allele. Immunoblotting studies, using a polyclonal **antibody** to the purified protein, showed an absence of immunoreactive protein in mitochondrial fractions prepared from fibroblasts from MCAD-deficient patients. To determine whether MCAD protein accumulated in the cytosol because of impaired transport into the mitochondria, we immunoprecipitated MCAD protein from the fibroblast homogenate. MCAD protein was detected in the immunoprecipitates from controls, but not in those from the MCAD-deficient patients. These results suggest that either the MCAD protein is not synthesised or, if produced, it is rapidly degraded.

L4 ANSWER 25 OF 34 MEDLINE DUPLICATE 11

92050975 Document Number: 92050975. PubMed ID: 1945557. Immunochemical characterization of variant long-chain **acyl-CoA dehydrogenase** in cultured fibroblasts from nine patients with long-chain **acyl-CoA dehydrogenase** deficiency. Indo Y; Coates P M; Hale D E; Tanaka K. (Yale University School of Medicine, Department of Human Genetics, New Haven, Connecticut 06510.) PEDIATRIC RESEARCH, (1991 Sep) 30 (3) 211-5. Journal code: 0100714. ISSN: 0031-3998. Pub. country: United States. Language: English.

AB Long-chain **acyl-CoA dehydrogenase** (LCAD) deficiency is a disorder of mitochondrial fatty acid oxidation that is characterized by hypoglycemia, muscle weakness, and hepato- and cardiomegaly. To characterize variant LCAD, we first carried out preliminary experiments using pure enzyme preparations. Despite the significant sequence similarity of LCAD to medium-chain **acyl-CoA dehydrogenase**, the **antibody** raised against rat LCAD was monospecific for **human** and rat LCAD and did not cross-react with either **human** or rat medium-chain **acyl-CoA dehydrogenase**. Immunoblot analysis of variant LCAD in cultured fibroblasts from nine patients with LCAD deficiency revealed a single LCAD band in all nine LCAD-deficient cell lines. Each variant LCAD was comparable in molecular size and quantity to normal LCAD, suggesting that the LCAD mutation in each of these cell lines is likely to be a point mutation that produces a stable variant LCAD. The uniform nature of variant LCAD suggests that only a single, or at most a few, prevalent point mutations may be found in the majority of LCAD-deficient

patients. If this is the case, it should be possible to devise a molecular diagnostic method for LCAD deficiency.

L4 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2002 ACS
1990:492277 Document No. 113:92277 Molecular cloning and nucleotide sequence of cDNAs encoding **human** short chain **acyl-CoA dehydrogenase** and study of the molecular basis of **human** short chain **acyl-CoA dehydrogenase** deficiency. Naito, Etsuo; Ozasa, Hisashi; Ikeda, Yasuyuki; Tanaka, Kay (Sch. Med., Yale Univ., New Haven, CT, 06510, USA). Prog. Clin. Biol. Res., Volume Date 1988, 321(Fatty Acid Oxid.: Clin., Biochem., Mol. Aspects), 625-32 (English) 1990. CODEN: PCBRD2. ISSN: 0361-7742.
AB As a first step in the study of the mol. basis of inherited short chain acyl-CoA dehdyrogenase (SCAD) deficiency and as part of a study on the structure/function relationships and evolutionary aspects of the **acyl-CoA dehydrogenase** family, the authors cloned and sequenced cDNAs encoding the entire **human** precursor of SCAD. In addn., they studied the protein and mRNA of the variant **human** SCAD and the restriction pattern of its gene in cultured skin fibroblasts from three patients with SCAD deficiency using a monospecific **antibody** and one of the isolated SCAD cDNA as probes.

L4 ANSWER 27 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 12
1990:495657 Document No.: BA90:124003. IMMUNOCHEMICAL AND MOLECULAR ANALYSIS OF MEDIUM-CHAIN ACYL COENZYME A DEHYDROGENASE DEFICIENCY. INAGAKI T; OHISHI N; BACHMANN C; GHISLA S; TSUKAGOSHI N; UDAKA S; YAGI K. INST. APPLIED BIOCHEM., YAGI MEMORIAL PARK, MITAKE, GIFU 505-01, JPN.. J CLIN BIOCHEM NUTR, (1990) 8 (1), 1-8. CODEN: JCBNER. ISSN: 0912-0009. Language: English.
AB Medium-chain **acyl CoA dehydrogenase** (MCAD) (acyl-CoA: (acceptor) 2,3-oxidoreductase, EC 1.3.99.3) deficiency in two patients, MV and AH, was examined by use of an anti-MCAD **antibody** and the cDNA for the enzyme. No MCAD protein was detected by immunoblot analysis in the fibroblast extract from the first patient MV, while it was present, but not catalytically active in the second patient AH. In order to clarify the molecular mechanism of these deficiencies, a cDNA encoding MCAD was isolated from a **human** placenta cDNA library. The cDNA contained 1,263 nucleotides of the coding region, 64 nucleotides of the 5'-noncoding region, and 686 nucleotides of the 3'-noncoding region. The level of mRNA for MCAD in the patients was examined by RNA blot analysis with the cDNA as probe, and the results indicate that the patient MV also had the mRNA and that the level of the mRNA in both patients was almost the same as that of the control subject. Thus it seems that the deficiency in the patients is due to a point mutation(s) and that the position of the mutation(s) in the gene of patient MV is different from that of patient AH.

L4 ANSWER 28 OF 34 MEDLINE DUPLICATE 13
89214689 Document Number: 89214689. PubMed ID: 2565344. Molecular cloning and nucleotide sequence of complementary DNAs encoding **human** short chain acyl-coenzyme A dehydrogenase and the study of the molecular basis of **human** short chain acyl-coenzyme A dehydrogenase deficiency. Naito E; Ozasa H; Ikeda Y; Tanaka K. (Department of Human Genetics, Yale University School of Medicine, New Haven, Connecticut 06510.) JOURNAL OF CLINICAL INVESTIGATION, (1989 May) 83 (5) 1605-13. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.
AB Complementary DNAs encoding the precursor of **human** placental short chain acyl-coenzyme A (CoA) dehydrogenase (SCAD) (EC 1.3.99.2) were cloned and sequenced. The cDNA inserts in these clones were 1,852 bases in length combined, and encoded the entire 412-amino acid precursor SCAD (mol

wt 44,303). This sequence included the 24-amino acid leader peptide moiety (mol wt 2,576) and 388 amino acids corresponding to the mature protein (mol wt 41,727). The comparison of SCAD and medium chain **acyl-CoA dehydrogenase** sequences revealed a high degree of homology, suggesting that these enzymes evolved from a common ancestral gene and belong to a gene family. We also studied mutant **human** SCAD in cultured skin fibroblasts from three patients with hereditary SCAD deficiency. Labeling fibroblast cultures with [35S]-methionine followed by immunoprecipitation with anti-SCAD **antibody** revealed that a normal size variant SCAD protein was synthesized. In all of the three SCAD-deficient cell lines, the size of variant SCAD mRNA as determined by Northern blotting using one of the normal SCAD cDNA as a probe was also normal, and no difference was observed on Southern blots in the restriction patterns of mutant genomic DNA using EcoRI, TaqI, HincII, and BamHI. These results suggest that the defects in SCAD in these cell lines are caused by a point mutation.

L4 ANSWER 29 OF 34 MEDLINE DUPLICATE 14

89372738 Document Number: 89372738. PubMed ID: 2774489. Normalization of short-chain acylcoenzyme A dehydrogenase after riboflavin treatment in a girl with multiple acylcoenzyme A dehydrogenase-deficient myopathy. DiDonato S; Gellera C; Peluchetti D; Uziel G; Antonelli A; Lus G; Rimoldi M. (Laboratory of Biochemistry and Genetics of the Nervous System, Instituto Neurologico C. Besta, Milan, Italy.) ANNALS OF NEUROLOGY, (1989 May) 25 (5) 479-84. Journal code: 7707449. ISSN: 0364-5134. Pub. country: United States. Language: English.

AB A 12-year-old girl was shown to have carnitine-deficient lipid storage myopathy and organic aciduria compatible with multiple acylcoenzyme A (**acyl-CoA**) **dehydrogenase** deficiency. In muscle mitochondria, activities of both short-chain **acyl-CoA dehydrogenase** (SCAD) and medium-chain **acyl-CoA dehydrogenase** (MCAD) were 35% of normal. **Antibodies** against purified SCAD, MCAD, and electron-transfer flavoprotein were used for detection of cross-reacting material (CRM) in the patient's mitochondria. Western blot analysis showed absence of SCAD-CRM, reduced amounts of MCAD-CRM, and normal amounts of electron-transfer flavoprotein-CRM. The patient, who was unresponsive to treatment with oral carnitine, improved dramatically with daily administration of 100 mg oral riboflavin. Increase in muscle bulk and strength and resolution of the organic aciduria were associated with normalization of SCAD activity and "reappearance" of SCAD-CRM. In contrast, both MCAD activity and MCAD-CRM remained lower than normal. These results suggest that in some patients with multiple **acyl-CoA dehydrogenase** deficiency riboflavin supplementation may be effective in restoring the activity of SCAD, and possibly of other mitochondrial flavin-dependent enzymes.

L4 ANSWER 30 OF 34 MEDLINE DUPLICATE 15

88087890 Document Number: 88087890. PubMed ID: 3335634. Genetic deficiency of short-chain acyl-coenzyme A dehydrogenase in cultured fibroblasts from a patient with muscle carnitine deficiency and severe skeletal muscle weakness. Coates P M; Hale D E; Finocchiaro G; Tanaka K; Winter S C. (Division of Genetics, Children's Hospital of Philadelphia, Pennsylvania 19104.) JOURNAL OF CLINICAL INVESTIGATION, (1988 Jan) 81 (1) 171-5. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB Genetic deficiency of short-chain acyl-coenzyme A (CoA) dehydrogenase activity was demonstrated in cultured fibroblasts from a 2-yr-old female whose early postnatal life was complicated by poor feeding, emesis, and failure to thrive. She demonstrated progressive skeletal muscle weakness and developmental delay. Her plasma total carnitine level (35 nmol/ml) was low-normal, but was esterified to an abnormal degree (55% vs. control of less than 10%). Her skeletal muscle total carnitine level was low (7.6

nmol/mg protein vs. control of 14 +/- 2 nmol/mg protein) and was 75% esterified. Mild lipid deposition was noted in type I muscle fibers. Fibroblasts from this patient had 50% of control levels of **acyl-CoA dehydrogenase** activity towards butyryl-CoA as substrate at a concentration of 50 muM in a fluorometric assay based on the reduction of electron transfer flavoprotein. All of this residual activity was inhibited by an **antibody** against medium-chain **acyl-CoA dehydrogenase**. These data demonstrated that medium-chain **acyl-CoA dehydrogenase** accounted for 50% of the activity towards the short-chain substrate, butyryl-CoA, under these conditions, but that **antibody** against that enzyme could be used to unmask the specific and virtually complete deficiency of short-chain **acyl-CoA dehydrogenase** in this patient. Fibroblasts from her parents had intermediate levels of activity towards butyryl-CoA, consistent with the autosomal recessive inheritance of this metabolic defect.

L4 ANSWER 31 OF 34 MEDLINE DUPLICATE 16

87271315 Document Number: 87271315. PubMed ID: 3606893. Immunoprecipitation and electrophoretic analysis of four **human acyl-CoA dehydrogenases** and electron transfer flavoprotein using **antibodies** raised against the corresponding rat enzymes. Ikeda Y; Tanaka K. BIOCHEMICAL MEDICINE AND METABOLIC BIOLOGY, (1987 Jun) 37 (3) 329-34. Journal code: 8605718. ISSN: 0885-4505. Pub. country: United States. Language: English.

AB We prepared monospecific antisera in rabbits against purified rat short-, medium-, and long-chain **acyl-CoA dehydrogenases**, isovaleryl-CoA dehydrogenase, and ETF and tested the immunocross-reactivity to the corresponding **human** enzymes. Each antiserum specifically reacted with the corresponding **human** enzyme. When immunoprecipitates were analyzed by SDS-PAGE, the mobilities of all the **human acyl-CoA dehydrogenases** and ETF subunits were identical to those of the rat counterparts with a single exception. **Human** medium-chain **acyl-CoA dehydrogenase** had a mobility on SDS-PAGE slightly slower than that of rat medium-chain **acyl-CoA dehydrogenase**, suggesting that **human** medium-chain **acyl-CoA dehydrogenase** was 1 kDa larger than the rat counterpart. The immunocross-reactivity of the antisera, raised against the rat **acyl-CoA dehydrogenases** and ETF to the **human** counterpart, provide useful tools for the study of mutant enzymes in cells from patients with a genetic defect of **acyl-CoA dehydrogenases** of ETF.

L4 ANSWER 32 OF 34 MEDLINE DUPLICATE 17

88186060 Document Number: 88186060. PubMed ID: 3446585. Isolation of cDNA clones coding for rat isovaleryl-CoA dehydrogenase and assignment of the gene to **human** chromosome 15. Kraus J P; Matsubara Y; Barton D; Yang-Feng T L; Glassberg R; Ito M; Ikeda Y; Mole J; Francke U; Tanaka K. (Department of Human Genetics, Yale University School of Medicine, New Haven, Connecticut 06510.) GENOMICS, (1987 Nov) 1 (3) 264-9. Journal code: 8800135. ISSN: 0888-7543. Pub. country: United States. Language: English.

AB Rat liver mRNA encoding the cytoplasmic precursor of mitochondrial isovaleryl-CoA dehydrogenase was highly enriched by polysome immunopurification using a polyclonal monospecific **antibody**. The purified mRNA was used to prepare a plasmid cDNA library which was screened with two oligonucleotide mixtures encoding two peptides in the amino-terminal portion of mature rat isovaleryl-CoA dehydrogenase. Thirty-one overlapping cDNA clones, spanning a region of 2.1 kbp, were isolated and characterized. The cDNA sequence of a 5'-end clone, rIVD-13

(155 bp), predicts a mitochondrial leader peptide of 30 amino acid residues and the first 18 amino acids of the mature protein. These consecutive 18 residues completely matched the amino-terminal peptide determined by automated Edman degradation of the rat enzyme. The leader peptide contains six arginines, has no acidic residues, and is particularly rich in leucine, alanine, and proline residues. Southern blot analysis of DNAs from **human**-rodent somatic cell hybrids with an isolated rat cDNA (2 kbp) assigned the isovaleryl-CoA dehydrogenase gene to the long arm of chromosome 15, region q14----qter. The chromosomal assignment was confirmed and further refined to bands q14----q15 by in situ hybridization of the probe to **human** metaphase cells. This location differs from that of the gene for medium-chain **acyl-CoA dehydrogenase**, a closely related enzyme, which has been previously assigned to chromosome 1.

L4 ANSWER 33 OF 34 MEDLINE DUPLICATE 18

86313614 Document Number: 86313614. PubMed ID: 3462713. Molecular cloning of cDNAs encoding rat and **human** medium-chain **acyl-CoA dehydrogenase** and assignment of the gene to **human** chromosome 1. Matsubara Y; Kraus J P; Yang-Feng T L; Francke U; Rosenberg L E; Tanaka K. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1986 Sep) 83 (17) 6543-7. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Rat liver mRNA encoding the precursor of medium-chain **acyl-CoA dehydrogenase** was purified to near homogeneity by polysome immunoadsorption using a polyclonal, monospecific **antibody**. A single-stranded, 32P-labeled cDNA probe was synthesized using the enriched mRNA as template and was used to screen directly 15,000 colonies from a total rat liver cDNA library constructed in pBR322. One clone [600 base pairs (bp)] was positively identified by hybrid-selected translation combined with mitochondrial processing of translated products. Using the isolated rat cDNA as probe, 43,000 colonies from a **human** liver cDNA library were screened. Three overlapping clones (1100 bp, 500 bp, and 400 bp) were isolated and positively identified by hybrid-selected translation. The largest **human** cDNA clone was subcloned into the transcription vector pGEM-2, which contains a bacteriophage T7 RNA polymerase promoter. In vitro transcription of this recombinant, followed by in vitro translation, showed that the cDNA clone coded for approximately 80% of the medium-chain **acyl-CoA dehydrogenase** protein. The sizes of rat and **human** mRNAs encoding the precursor of medium-chain **acyl-CoA dehydrogenase** were 2.2 and 2.4 kilobases long, respectively, as determined by blot hybridization analysis of electrophoretically fractionated poly(A)+ RNA. Southern blot analysis of DNAs from **human**-rodent somatic cell hybrids with an isolated **human** cDNA assigned the gene coding for this enzyme to the short arm of chromosome 1, band p31. The chromosomal assignment was confirmed by in situ hybridization of the probe to **human** metaphase cells. Direct screening of cDNA libraries using a highly enriched mRNA to generate a probe, as demonstrated in this study, may provide the most rapid and convenient approach to cDNA cloning of low-abundance mRNAs.

L4 ANSWER 34 OF 34 MEDLINE DUPLICATE 19

86312625 Document Number: 86312625. PubMed ID: 3748657. Biosynthesis of variant medium chain **acyl-CoA dehydrogenase** in cultured fibroblasts from patients with medium chain **acyl-CoA dehydrogenase** deficiency. Ikeda Y; Hale D E; Keese S M; Coates P M; Tanaka K. PEDIATRIC RESEARCH, (1986 Sep) 20 (9) 843-7. Journal code: 0100714. ISSN: 0031-3998. Pub. country: United States. Language: English.

AB We prepared monospecific antiserum in rabbits against medium chain **acyl-CoA dehydrogenase** (MCAD) purified from

rat liver and studied the biosynthesis of MCAD in cultured skin fibroblasts from patients with MCAD deficiency using the **antibody** . Cells were incubated with [35S]methionine. The labeled MCAD was immunoprecipitated using the anti-rat MCAD antiserum and Staphylococcus aureus cells and then analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. We first demonstrated that antirat MCAD **antibody** crossreacted specifically with **human** MCAD. In 13 MCAD-deficient cell lines tested, the residual MCAD activity ranged from 5-12% of the mean of normal controls, but the variant MCAD in all of these cells was indistinguishable from the normal **human** MCAD on the basis of molecular size, indicating that MCAD deficiency in all of these patients is most likely due to point mutation(s) in the MCAD gene.

```
=> d his

     (FILE 'HOME' ENTERED AT 12:00:19 ON 01 AUG 2002)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 12:00:30 ON
     01 AUG 2002
L1      2331124 S ANTIBODY
L2          142 S L1 AND ACYL COA DEHYDROGENASE
L3           85 S L2 AND HUMAN
L4           34 DUP REMOVE L3 (51 DUPLICATES REMOVED)

=> s l2 and c elegan
L5            0 L2 AND C ELEGAN

=> s l2 and yeast
L6            1 L2 AND YEAST

=> d l6 cbib abs

L6   ANSWER 1 OF 1  SCISEARCH  COPYRIGHT 2002 ISI (R)
94:96857   The Genuine Article (R) Number: MW989. INTRAMITOCHONDRIAL FOLDING
     AND ASSEMBLY OF MEDIUM-CHAIN ACYL-COA
     DEHYDROGENASE (MCAD) - DEMONSTRATION OF IMPAIRED TRANSFER OF
     K304E-VARIANT MCAD FROM ITS COMPLEX WITH HSP60 TO THE NATIVE TETRAMER.
     SAIJO T; WELCH W J; TANAKA K (Reprint). YALE UNIV, SCH MED, DEPT GENET,
     333 CEDAR ST, POB 3333, NEW HAVEN, CT, 06510 (Reprint); YALE UNIV, SCH
     MED, DEPT GENET, NEW HAVEN, CT, 06510; UNIV CALIF SAN FRANCISCO, DEPT MED,
     SAN FRANCISCO, CA, 94143; UNIV CALIF SAN FRANCISCO, DEPT PHYSIOL, SAN
     FRANCISCO, CA, 94143. JOURNAL OF BIOLOGICAL CHEMISTRY (11 FEB 1994) Vol.
     269, No. 6, pp. 4401-4408. ISSN: 0021-9258. Pub. country: USA. Language:
     ENGLISH.
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB      We incubated in vitro translated precursor of medium-chain acyl
     -CoA dehydrogenase (MCAD) with isolated rat liver
     mitochondria and fractionated the solubilized mitochondria on gel
     filtration. After a 5-min import into mitochondria, MCAD was recovered
     exclusively as a high molecular weight (hM(r)) complex (700,000), while
     after a 10 min import, it was recovered mainly in the hM(r) complex and
     mature tetramer, with a small amount in monomer. Either a further 15-min
     chase or exposure to ATP caused a marked decrease of MCAD in the hM(r)
     complex and an increase in the mature tetramer in comparable amounts,
     suggesting that the hM(r) complex was the precursor of tetramer. No
     monomer was detected in either case. Using specific antibodies,
     we have shown that the hM(r) complex represented a complex of MCAD and
     heat shock protein 60 (hsp60), and, that upon import into mitochondria,
     unfolded MCAD first formed a transient complex with mitochondrial
     heat-shock protein 70 (hsp70(mit)) and then transferred to hsp60 to
     complete its folding into an assembly-competent conformation. We also
     examined the assembly of K304E MCAD, which is a prevalent variant enzyme
```

among patients with MCAD deficiency. The assembly of the K304E into its tetrameric form was severely impaired. The binding of K304E with hsp70(mit) and its transfer from hsp70(mit) to hsp60 were normal. However, the hsp60 complex of K304E was much more stable than the wild-type counterpart upon a 15-min chase or exposure to ATP, suggesting that the folding in, or the transfer of K304E subunit to tetramer from, the complex with hsp60 was impaired.

=> s l2 and (lal P?/au or corely n?/au)
L7 1 L2 AND (LAL P?/AU OR CORELY N?/AU)

=> d l7 cbib abs

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
1999:468022 Document No. 131:99271 Cloning and cDNA sequence of human short-chain dehydrogenase. **Lal, Preeti**; Corley, Neil C. (Incyte Pharmaceuticals, Inc., USA). U.S. US 5928923 A 19990727, 27 pp. (English). CODEN: USXXAM. APPLICATION: US 1998-19216 19980205.
AB The invention provides a human short-chain dehydrogenase (HSCD) and polynucleotides which identify and encode HSCD. Nucleic acids encoding HSCD were first identified in Incyte clone 365351 from a prostate cDNA library using a computer search for amino acid sequence alignments; a consensus sequence was derived from overlapping and/or extended nucleic acid sequences. HSCD is 313 amino acids in length and has 4 potential casein kinase II phosphorylation sites, one potential glycosaminoglycan attachment site, one potential microbodies C-terminal targeting signal site, 4 potential N-myristoylation sites, and 5 potential protein kinase C phosphorylation sites, as well as chem. and structural homol. with short-chain **acyl-CoA dehydrogenase**.
Northern anal. shows the expression of this sequence in various libraries, at least 50% of which are immortalized or cancerous and .gtoreq.27% of which involve the immune response. The invention also provides expression vectors, host cells, **antibodies**, agonists, and antagonists. The invention also provides methods for treating or preventing disorders assocd. with expression of HSCD.

=> s (lal p?/au or corley n?/au)
L8 1250 (LAL P?/AU OR CORLEY N?/AU)

=> s l8 and short chain dehydrogenase
L9 3 L8 AND SHORT CHAIN DEHYDROGENASE

=> dup remove l9 cbib abs
'CBIB' IS NOT VALID. VALID FILE NAMES ARE 'BIOSIS, CAPLUS'
You have entered a file name of duplicates to keep that is not referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10 2 DUP REMOVE L9 (1 DUPLICATE REMOVED)

=> d l10 1-2 cbib abs

L10 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:337513 Document No.: PREV200200337513. Human **short-chain dehydrogenase. Lal, Preeti; Corley, Neil C.**. ASSIGNEE: Incyte Genomics, Inc.. Patent Info.: US 6387613 May 14, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (May 14, 2002) Vol. 1258, No. 2, pp. No Pagination.

http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133. Language: English.

AB The invention provides a human **short-chain dehydrogenase** (HSCD) and polynucleotides which identify and encode HSCD. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for treating or preventing disorders associated with expression of HSCD.

L10 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
1999:443861 Document No.: PREV199900443861. Human **short-chain dehydrogenase. Lal, Preeti (1)**; **Corley, Neil C.**. (1) Molecular Dynamics, Sunnyvale, CA USA. ASSIGNEE: Incyte Pharmaceuticals, Inc.. Patent Info.: US 5928923 Jul. 27, 1999. Official Gazette of the United States Patent and Trademark Office Patents, (Jul. 27, 1999) Vol. 1224, No. 4, pp. NO PAGINATION. ISSN: 0098-1133. Language: English.

=> d his

(FILE 'HOME' ENTERED AT 12:00:19 ON 01 AUG 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 12:00:30 ON 01 AUG 2002

```
L1      2331124 S ANTIBODY
L2          142 S L1 AND ACYL COA DEHYDROGENASE
L3           85 S L2 AND HUMAN
L4           34 DUP REMOVE L3 (51 DUPLICATES REMOVED)
L5            0 S L2 AND C ELEGAN
L6            1 S L2 AND YEAST
L7            1 S L2 AND (LAL P?/AU OR CORELY N?/AU)
L8         1250 S (LAL P?/AU OR CORLEY N?/AU)
L9            3 S L8 AND SHORT CHAIN DEHYDROGENASE
L10           2 DUP REMOVE L9 (1 DUPLICATE REMOVED)
```

```
=> s l2 and caenohabditis elegans
L11           0 L2 AND CAENOHABDITIS ELEGANS

=> s "HSCD"
L12          31 "HSCD"

=> s l12 and antibod?
L13           2 L12 AND ANTIBOD?

=> dup remove l13
PROCESSING COMPLETED FOR L13
L14           2 DUP REMOVE L13 (0 DUPLICATES REMOVED)

=> d l14 1-2 cbib abs
```

L14 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:337513 Document No.: PREV200200337513. Human short-chain dehydrogenase. Lal, Preeti; Corley, Neil C.. ASSIGNEE: Incyte Genomics, Inc.. Patent Info.: US 6387613 May 14, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (May 14, 2002) Vol. 1258, No. 2, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133. Language: English.

AB The invention provides a human short-chain dehydrogenase (**HSCD**) and polynucleotides which identify and encode **HSCD**. The invention also provides expression vectors, host cells, **antibodies**, agonists, and antagonists. The invention also provides methods for treating or preventing disorders associated with expression of **HSCD**.

L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
1999:468022 Document No. 131:99271 Cloning and cDNA sequence of human short-chain dehydrogenase. Lal, Preeti; Corley, Neil C. (Incyte Pharmaceuticals, Inc., USA). U.S. US 5928923 A 19990727, 27 pp. (English). CODEN: USXXAM. APPLICATION: US 1998-19216 19980205.

AB The invention provides a human short-chain dehydrogenase (**HSCD**) and polynucleotides which identify and encode **HSCD**. Nucleic acids encoding **HSCD** were first identified in Incyte clone 365351 from a prostate cDNA library using a computer search for amino acid sequence alignments; a consensus sequence was derived from overlapping and/or extended nucleic acid sequences. **HSCD** is 313 amino acids in length and has 4 potential casein kinase II phosphorylation sites, one potential glycosaminoglycan attachment site, one potential microbodies C-terminal targeting signal site, 4 potential N-myristoylation sites, and 5 potential protein kinase C phosphorylation sites, as well as chem. and structural homol. with short-chain acyl-CoA dehydrogenase. Northern anal. shows the expression of this sequence in various libraries, at least 50% of which are immortalized or cancerous and .gtoreq.27% of which involve the immune response. The invention also provides expression vectors, host cells, **antibodies**, agonists, and antagonists. The invention also provides methods for treating or preventing disorders assocd. with expression of **HSCD**.

=> dup remove l12
PROCESSING COMPLETED FOR L12
L15 13 DUP REMOVE L12 (18 DUPLICATES REMOVED)

=> d l15 1-13 cbib abs

L15 ANSWER 1 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:337513 Document No.: PREV200200337513. Human short-chain dehydrogenase. Lal, Preeti; Corley, Neil C.. ASSIGNEE: Incyte Genomics, Inc.. Patent Info.: US 6387613 May 14, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (May 14, 2002) Vol. 1258, No. 2, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133. Language: English.

AB The invention provides a human short-chain dehydrogenase (**HSCD**) and polynucleotides which identify and encode **HSCD**. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for treating or preventing disorders associated with expression of **HSCD**.

L15 ANSWER 2 OF 13 MEDLINE DUPLICATE 1
2000195114 Document Number: 20195114. PubMed ID: 10732976. Syntheses of R and S isomers of AF-DX 384, a selective antagonist of muscarinic M2 receptors. Martin J; Deagostino A; Perrio C; Dauphin F; Ducandas C; Morin C; Desbene P L; Lasne M C. (Laboratoire de Chimie Moleculaire et Thio-organique, (CNRS UMR 6507), Institut des Sciences de la Matiere et du Rayonnement, Caen, France.) BIOORGANIC AND MEDICINAL CHEMISTRY, (2000 Mar) 8 (3) 591-600. Journal code: 9413298. ISSN: 0968-0896. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Enantiomers of 5,11-dihydro-11-[2-[2-[(N,N-dipropylaminomethyl)piperidin-1-yl]ethylamino]-carbonyl]-6H-pyrido[2,3-b][1,4]benzodiazepin-6-one (AF-DX 384) 1, have been synthesized from (S)-(+) and (R)-(-)-2-[N,N-dipropylaminomethyl]piperidine 4. The enantiomeric excess of 1 has been determined by capillary electrophoresis by using the alpha-highly sulphated cyclodextrin (alpha-**HSCD**) as chiral selector within the running electrolyte. (S)-(+)-(4) was prepared from (S)-(-)-pipecolic acid in a 4-step procedure (overall yield: 30%, ee: 99%) and (R)-(-)-AF-DX 384 from (R)-(+)-pipecolic acid. The (R)-(-) isomer exhibited in vitro a

23-fold higher affinity than its enantiomer (S)-(+) towards muscarinic receptors of subtype 2.

L15 ANSWER 3 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
2000:437731 The Genuine Article (R) Number: 321AE. Hardware and compiler-directed cache coherence in large-scale multiprocessors: Design considerations and performance study. Choi L (Reprint); Yew P C. UNIV CALIF IRVINE, DEPT ELECT & COMP ENGN, IRVINE, CA 92697 (Reprint); UNIV MINNESOTA, DEPT COMP SCI, MINNEAPOLIS, MN 55455. IEEE TRANSACTIONS ON PARALLEL AND DISTRIBUTED SYSTEMS (APR 2000) Vol. 11, No. 4, pp. 375-394. Publisher: IEEE-INST ELECTRICAL ELECTRONICS ENGINEERS INC. 345 E 47TH ST, NEW YORK, NY 10017-2394. ISSN: 1045-9219. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB In this paper, we study a hardware-supported, compiler-directed (**HSCD**) cache coherence scheme, which can be implemented on a large-scale multiprocessor using off-the-shelf microprocessors, such as the Gray T3D. The scheme can be adapted to various cache organizations, including multiword cache lines and byte-addressable architectures. Several system related issues, including critical sections, interthread communication, and task migration have also been addressed. The cost of the required hardware support is minimal and proportional to the cache size. The necessary compiler algorithms, including intra- and interprocedural array data flow analysis, have been implemented on the Polaris parallelizing compiler [34]. From our simulation study using the Perfect Club benchmarks [5], we found that in spite of the conservative analysis made by the compiler, for four of six benchmark programs tested, the proposed **HSCD** scheme outperforms the full-map hardware directory scheme up to 70 percent while the hardware scheme outperforms the **HSCD** scheme in the remaining two applications up to 89 percent. Given its comparable performance and reduced hardware cost, the proposed scheme can be a viable alternative for large-scale multiprocessors such as the Gray T3D, which rely on users to maintain data coherence.

L15 ANSWER 4 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
1999:443861 Document No.: PREV199900443861. Human short-chain dehydrogenase. Lal, Preeti (1); Corley, Neil C.. (1) Molecular Dynamics, Sunnyvale, CA USA. ASSIGNEE: Incyte Pharmaceuticals, Inc.. Patent Info.: US 5928923 Jul. 27, 1999. Official Gazette of the United States Patent and Trademark Office Patents, (Jul. 27, 1999) Vol. 1224, No. 4, pp. NO PAGINATION. ISSN: 0098-1133. Language: English.

L15 ANSWER 5 OF 13 MEDLINE DUPLICATE 3
1998281700 Document Number: 98281700. PubMed ID: 9620390. Rapid extraction of genomic DNA from medically important yeasts and filamentous fungi by high-speed cell disruption. Muller F M; Werner K E; Kasai M; Francesconi A; Chanock S J; Walsh T J. (Immunocompromised Host Section, Pediatric Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.. frank.mueller@mail.uni-wuerzburg.de) . JOURNAL OF CLINICAL MICROBIOLOGY, (1998 Jun) 36 (6) 1625-9. Journal code: 7505564. ISSN: 0095-1137. Pub. country: United States. Language: English.
AB Current methods of DNA extraction from different fungal pathogens are often time-consuming and require the use of toxic chemicals. DNA isolation from some fungal organisms is difficult due to cell walls or capsules that are not readily susceptible to lysis. We therefore investigated a new and rapid DNA isolation method using high-speed cell disruption (**HSCD**) incorporating chaotropic reagents and lysing matrices in comparison to standard phenol-chloroform (PC) extraction protocols for isolation of DNA from three medically important yeasts (Candida albicans, Cryptococcus neoformans, and Trichosporon beigelii) and two filamentous fungi

(Aspergillus fumigatus and Fusarium solani). Additional extractions by **HSCD** were performed on Saccharomyces cerevisiae, Pseudallescheria boydii, and Rhizopus arrhizus. Two different inocula (10(8) and 10(7) CFU) were compared for optimization of obtained yields. The entire extraction procedure was performed on as many as 12 samples within 1 h compared to 6 h for PC extraction. In comparison to the PC procedure, **HSCD** DNA extraction demonstrated significantly greater yields for 10(8) CFU of C. albicans, T. beigelii, A. fumigatus, and F. solani ($P < or = 0.005$), 10(7) CFU of C. neoformans ($P < or = 0.05$), and 10(7) CFU of A. fumigatus ($P < or = 0.01$). Yields were within the same range for 10(8) CFU of C. neoformans and 10(7) CFU of C. albicans for both **HSCD** extraction and PC extraction. For 10(7) CFU of T. beigelii, PC extraction resulted in a greater yield than did **HSCD** ($P < or = 0.05$). Yields obtained from 10(8) and 10(7) CFU were significantly greater for filamentous fungi than for yeasts by the **HSCD** extraction procedure ($P < 0.0001$). By the PC extraction procedure, differences were not significant. For all eight organisms, the rapid extraction procedure resulted in good yield, integrity, and quality of DNA as demonstrated by restriction fragment length polymorphism, PCR, and random amplified polymorphic DNA. We conclude that mechanical disruption of fungal cells by **HSCD** is a safe, rapid, and efficient procedure for extracting genomic DNA from medically important yeasts and especially from filamentous fungi.

L15 ANSWER 6 OF 13 MEDLINE DUPLICATE 4

91193853 Document Number: 91193853. PubMed ID: 1707451. Eosinophilic granuloma of the bone in Hand-Schuller-Christian disease: extensive in vivo eosinophil degranulation and subsequent binding of released eosinophil peroxidase (EPO) to other inflammatory cells. Zabucchi G; Soranzo M R; Menegazzi R; Cattin L; Vecchio M; Lanza F; Patriarca P. (Istituto di Patologia Generale, Universita di Trieste, Italy.) JOURNAL OF PATHOLOGY, (1991 Mar) 163 (3) 225-31. Journal code: 0204634. ISSN: 0022-3417. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The eosinophils from bone granuloma, bone marrow, and peripheral blood of a patient with Hand-Schuller-Christian disease (**HSCD**) were studied by electron microscopy and cytochemistry. Impressive eosinophil degranulation was observed. Extracellular release of eosinophil peroxidase (EPO) and EPO binding to surrounding cells were seen in the granuloma and bone marrow. Cells with peroxidase-positive plasma membrane were also observed in peripheral blood. The pattern of eosinophil degranulation showed quite different features from those described so far. In the granuloma, the process begins with intracytoplasmic release of the granule matrix content, as revealed by both extensive extragranular accumulation of EPO and progressive decrease of the matrix electron density. Core dissolution follows thereafter, leading to complete disappearance of the granules. At the end of the process, the cells show rupture of the plasma membrane and release of their content into the surrounding environment. This pattern of secretion was also observed in blood and marrow eosinophils of the patient. In view of the previously reported findings that EPO binding to inflammatory cells influences their functions, EPO release and binding to surrounding cells in **HSCD** may play a role in the evolution of the inflammatory lesion in the disease.

L15 ANSWER 7 OF 13 MEDLINE DUPLICATE 5

92097058 Document Number: 92097058. PubMed ID: 1756492. Translocation (3;21) characterizes crises in myeloid stem cell disorders. Chen Z; Morgan R; Baer M R; Ligorsky R; Sandberg A A. (Cancer Center of Southwest Biomedical Research Institute, Scottsdale, Arizona 85251.) CANCER GENETICS AND CYTOGENETICS, (1991 Dec) 57 (2) 153-9. Journal code: 7909240. ISSN: 0165-4608. Pub. country: United States. Language: English.

AB Three patients, one with Philadelphia (Ph) chromosome positive chronic myelocytic leukemia (CML) and two with primary acquired myelodysplastic syndromes (MDS), have been identified to have a t(3;21)(q26;q22). In the patient with CML, the t(3;21) was detected only in the blast phase. The

t(3;21) as the sole abnormality appeared at presentation of MDS [refractory anemia with excess blasts (RAEB)] in one patient and remained as such when progression to RAEB in transformation (RAEB-t) occurred. The other patient with MDS had the t(3;21), in addition to other changes, during the progression of the disease. Thus, t(3;21) may characterize myeloid crises of clonal hematopoietic stem cell disorders (**HSCD**) and indicates a poor prognosis. As a primary cytogenetic event it may be also involved in the genesis of myelodysplasia with subsequent leukemic transformation.

L15 ANSWER 8 OF 13 MEDLINE DUPLICATE 6
91195892 Document Number: 91195892. PubMed ID: 2084900. [Cardiac changes in hereditary spinocerebellar degenerations]. Izmeneniia serdtsa pri nasledstvennykh spinotserebelliarnykh degeneratsiiakh. Illarioshkin S N; Borisenko V V; Ivanova-Smolenskaia I A. TERAPEVTICHESKII ARKHIV, (1990) 62 (10) 88-92. Journal code: 2984818R. ISSN: 0040-3660. Pub. country: USSR. Language: Russian.
AB Echocardiographic alterations were compared with the clinical picture in 32 patients with different forms of hereditary spinocerebellar degenerations (**HSCD**). Three groups of patients were examined. Group I included patients with Friedreich's ataxia (FA), group II consisted of patients with familial cerebellar degeneration, and group III of those with sporadic cerebellar degeneration. Echographic alterations associated with FA were recorded in 71.4% of cases. Cardiomyopathy was confirmed to be a characteristic feature of FA. Echographic alterations in FA were noted to be pleomorphic: apart from typical hypertrophy of the myocardium, a considerable enlargement of the left ventricle was detectable more seldom. In familial cerebellar degeneration, different echocardiographic alterations were recorded in 81.8% of cases, whereas in sporadic cerebellar degeneration, in 78.6% of cases. Dilated cardiomyopathy was revealed in 3 cases (in patients belonging to groups II and III). It is assumed that cardiac pathology may be one of the extraneural manifestations not only in FA but also in other forms of **HSCD**.

L15 ANSWER 9 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
91:5762 The Genuine Article (R) Number: EJ537. CARDIAC ALTERATIONS IN HEREDITARY SPINOCEREBELLAR DEGENERATIONS. ILLARIOSHKIN S N (Reprint); BORISENKO V V; IVANOVASMOLENSKAYA I A. ACAD MED SCI USSR, NEUROL RES INST, MOSCOW 109801, USSR (Reprint). TERAPEVTICHESKII ARKHIV (1990) Vol. 62, No. 10, pp. 88. Pub. country: USSR. Language: Russian.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Echocardiographic alterations were compared with the clinical picture in 32 patients with different forms of hereditary spinocerebellar degenerations (**HSCD**). Three groups of patients were examined. Group I included patients with Friedreich's ataxia (FA), group II consisted of patients with familial cerebellar degeneration, and group III of those with sporadic cerebellar degeneration. Echographic alterations associated with FA were recorded in 71.4% of cases. Cardiomyopathy was confirmed to be a characteristic feature of FA. Echographic alterations in FA were noted to be pleomorphic: apart from typical hypertrophy of the myocardium, a considerable enlargement of the left ventricle was detectable more seldom. In familial cerebellar degeneration, different echocardiographic alterations were recorded in 81.8% of cases, whereas in sporadic cerebellar degeneration, in 78.6% of cases. Dilated cardiomyopathy was revealed in 3 cases (in patients belonging to groups II and III). It is assumed that cardiac pathology may be one of the extraneural manifestations not only in FA but also in other forms of **HSCD**.

L15 ANSWER 10 OF 13 MEDLINE DUPLICATE 7
90015571 Document Number: 90015571. PubMed ID: 2507952. Growth hormone responses to growth hormone-releasing hormone in Hand-Schuller-Christian

Disease. Gelato M C; Loriaux D L; Merriam G R. (Developmental Endocrinology Branch, NICHHD, Bethesda, Md.) NEUROENDOCRINOLOGY, (1989 Sep) 50 (3) 259-64. Journal code: 0035665. ISSN: 0028-3835. Pub. country: Switzerland. Language: English.

AB Bolus doses of GH-releasing hormone (GHRH), 1 microgram/kg i.v., were given to two groups of adult patients with growth hormone deficiency (GHD): 9 with Hand-Schuller-Christian disease (**HSCD**, presumed hypothalamic GHD) and 9 with idiopathic GHD (IGHD, etiology unknown). Six patients in each group were then given further GHRH doses daily for 5 days, and the GH responses to GHRH were measured over 3 h on day 1 and day 5. Plasma levels of insulin-like growth factor-I (IGF-I) were measured twice daily on days 1 and 5 during GHRH treatment. All patients with **HSCD** had measurable GH responses to the first dose of GHRH, with a mean peak response of 6.4 +/- 2.1 ng/ml (mean +/- SE). Only 5 of 9 patients with IGHD had GH responses above the detection limits of the assay; their mean peak response, 1.3 +/- 0.2 ng/ml, was significantly lower than the GH responses of the **HSCD** patients (p less than 0.05). Responses in both groups of patients were lower than those previously observed in normal adult men (35 +/- 8 ng/ml; p less than 0.01). Five days of daily stimulation with GHRH significantly (p less than 0.01) increased the GH response in both groups of patients. The rise was greater in patients with **HSCD** than with IGHD (**HSCD**, 5.1 +/- 2.5 ng/ml on day 1, vs. 12.0 +/- 6.8 ng/ml on day 5; IGHD, 1.4 +/- 0.3 ng/ml vs. 2.9 +/- 0.6 ng/ml).(ABSTRACT TRUNCATED AT 250 WORDS)

L15 ANSWER 11 OF 13 MEDLINE DUPLICATE 8

82014403 Document Number: 82014403. PubMed ID: 7279345. Histiocytosis X and pregnancy. Ogburn P L Jr; Cefalo R C; Nagel T; Okagaki T. OBSTETRICS AND GYNECOLOGY, (1981 Oct) 58 (4) 513-5. Journal code: 0401101. ISSN: 0029-7844. Pub. country: United States. Language: English.

AB Histiocytosis X is associated with a pathologic proliferation of mononuclear histiocytes in the reticular endothelial system. Different clinical manifestations of this group of disorders may occur. Pregnancy and histiocytosis X infrequently occur simultaneously. Four cases previously reported along with 1 new case of histiocytosis X and pregnancy are reviewed in this report. Only chronic histiocytosis X, Hand-Schuller-Christian disease (**HSCD**), has been reported to occur during pregnancy. The most frequent complication during pregnancy was the onset or exacerbation of diabetes insipidus, as frequently seen with this disorder. The possibility that **HSCD** may alter pituitary function may contribute to the infrequent occurrence of pregnancy in patients with this disorder.

L15 ANSWER 12 OF 13 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

82008114 EMBASE Document No.: 1982008114. Histiocytosis X and pregnancy. Ogburn Jr. P.L.; Cefalo R.C.; Nagel T.; Okagaki T.. Dept. Obstet. Gynecol., Div. Matern. Fetal Med., Univ. North Carolina Sch. Med., Chapel Hill, NC, United States. Obstetrics and Gynecology 58/4 (513-515) 1981. CODEN: OBGNAS. Pub. Country: United States. Language: English.

AB Histiocytosis X is associated with a pathologic proliferation of mononuclear histiocytes in the reticular endothelial system. Different clinical manifestations of this group of disorders may occur. Pregnancy and histiocytosis X infrequently occur simultaneously. Four cases previously reported along with 1 new case of histiocytosis X and pregnancy are reviewed in this report. Only chronic histiocytosis X, Hand-Schueller-Christian disease (**HSCD**), has been reported to occur during pregnancy. The most frequent complication during pregnancy was the onset or exacerbation of diabetes insipidus, as frequently seen with this disorder. The possibility that **HSCD** may alter pituitary function may contribute to the infrequent occurrence of pregnancy in patients with this disorder.

L15 ANSWER 13 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)

81:512084 The Genuine Article (R) Number: MM858. APPLICATION OF SODIUM INFUSER TO THE HIGH SODIUM CONCENTRATION DIALYSIS (**HSCD**). URANO H (Reprint); IKEDA Y; HOSHINA S; NAKAMURA H; FURUKAWA M; ENDO K; NAKAGAWA I; TAJIRI M; SUZUKI M; HIRASAWA Y; NODA T; SANADA M. ARTIFICIAL ORGANS (1981) Vol. 5, No. 3, pp. 305. Language: ENGLISH.

=> d his

(FILE 'HOME' ENTERED AT 12:00:19 ON 01 AUG 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 12:00:30 ON 01 AUG 2002

```
L1      2331124 S ANTIBODY
L2          142 S L1 AND ACYL COA DEHYDROGENASE
L3           85 S L2 AND HUMAN
L4           34 DUP REMOVE L3 (51 DUPLICATES REMOVED)
L5            0 S L2 AND C ELEGAN
L6            1 S L2 AND YEAST
L7            1 S L2 AND (LAL P?/AU OR CORELY N?/AU)
L8         1250 S (LAL P?/AU OR CORLEY N?/AU)
L9            3 S L8 AND SHORT CHAIN DEHYDROGENASE
L10           2 DUP REMOVE L9 (1 DUPLICATE REMOVED)
L11           0 S L2 AND CAENOHABDITIS ELEGANS
L12          31 S "HSCD"
L13           2 S L12 AND ANTIBOD?
L14           2 DUP REMOVE L13 (0 DUPLICATES REMOVED)
L15          13 DUP REMOVE L12 (18 DUPLICATES REMOVED)

=> s l12 and chimeric
L16           0 L12 AND CHIMERIC

=> s l12 and fragment
L17           5 L12 AND FRAGMENT

=> s l17 and dup
L18           0 L17 AND DUP

=> dup remove l17
PROCESSING COMPLETED FOR L17
L19           1 DUP REMOVE L17 (4 DUPLICATES REMOVED)

=> d l19 cbib abs
```

L19 ANSWER 1 OF 1 MEDLINE DUPLICATE 1

1998281700 Document Number: 98281700. PubMed ID: 9620390. Rapid extraction of genomic DNA from medically important yeasts and filamentous fungi by high-speed cell disruption. Muller F M; Werner K E; Kasai M; Francesconi A; Chanock S J; Walsh T J. (Immunocompromised Host Section, Pediatric Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.. frank.mueller@mail.uni-wuerzburg.de) . JOURNAL OF CLINICAL MICROBIOLOGY, (1998 Jun) 36 (6) 1625-9. Journal code: 7505564. ISSN: 0095-1137. Pub. country: United States. Language: English.

AB Current methods of DNA extraction from different fungal pathogens are often time-consuming and require the use of toxic chemicals. DNA isolation from some fungal organisms is difficult due to cell walls or capsules that are not readily susceptible to lysis. We therefore investigated a new and rapid DNA isolation method using high-speed cell disruption (**HSCD**) incorporating chaotropic reagents and lysing matrices in comparison to standard phenol-chloroform (PC) extraction protocols for isolation of DNA from three medically important yeasts (Candida albicans, Cryptococcus neoformans, and Trichosporon beigelii) and two filamentous fungi

(Aspergillus fumigatus and Fusarium solani). Additional extractions by **HSCD** were performed on Saccharomyces cerevisiae, Pseudallescheria boydii, and Rhizopus arrhizus. Two different inocula (10(8) and 10(7) CFU) were compared for optimization of obtained yields. The entire extraction procedure was performed on as many as 12 samples within 1 h compared to 6 h for PC extraction. In comparison to the PC procedure, **HSCD** DNA extraction demonstrated significantly greater yields for 10(8) CFU of C. albicans, T. beigelii, A. fumigatus, and F. solani (P < or = 0.005), 10(7) CFU of C. neoformans (P < or = 0.05), and 10(7) CFU of A. fumigatus (P < or = 0.01). Yields were within the same range for 10(8) CFU of C. neoformans and 10(7) CFU of C. albicans for both **HSCD** extraction and PC extraction. For 10(7) CFU of T. beigelii, PC extraction resulted in a greater yield than did **HSCD** (P < or = 0.05). Yields obtained from 10(8) and 10(7) CFU were significantly greater for filamentous fungi than for yeasts by the **HSCD** extraction procedure (P < 0.0001). By the PC extraction procedure, differences were not significant. For all eight organisms, the rapid extraction procedure resulted in good yield, integrity, and quality of DNA as demonstrated by restriction **fragment** length polymorphism, PCR, and random amplified polymorphic DNA. We conclude that mechanical disruption of fungal cells by **HSCD** is a safe, rapid, and efficient procedure for extracting genomic DNA from medically important yeasts and especially from filamentous fungi.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	120.74	120.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-7.43	-7.43

STN INTERNATIONAL LOGOFF AT 12:11:02 ON 01 AUG 2002